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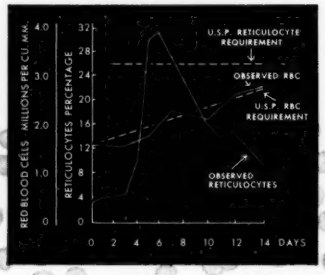

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VOLUME 97 NOVEMBER, 1953 NUMBER 5

INTRA-ARTERIAL AND INTRAVENOUS TRANSFUSION

A Controlled Study of Their Effectiveness in the Treatment of Experimental Hemorrhagic Shock

JAMES V. MALONEY, JR., M.D., Baltimore, Maryland, CHEVES McC. SMYTHE, M.D., JOSEPH P. GILMORE, M.S., and STANLEY W. HANDFORD, Ph.D., Camp Lejeune, North Carolina

THE success of intra-arterial transfusion (IAT) in the treatment of hemorrhagic shock is described in more than 60 recent clinical reports. The emergency nature of those clinical situations dire enough to require IAT does not create an atmosphere which enables the physician to determine the exact physiologic mechanism by which IAT exerts its beneficial effect on the circulation. The present study is an effort to evaluate IAT, and to compare it with intravenous transfusion (IVT), under controlled conditions in dogs.

Clinical experience and experimental study have led to the suggestion of a number of mechanisms to explain the apparent superiority of the intra-arterial over the intravenous route for whole blood transfusion. These explanations are that:

1. Direct introduction of blood under pressure into the arterial tree causes, by a hydraulic effect, an instantaneous rise in pressure through the arterial system.

2. IAT effects a more rapid recovery of arterial pressure in hemorrhagic shock with smaller transfusions.

3. Blood injected intra-arterially mixes immediately with that of the general circulation, whereas when given intravenously it may remain pooled in sluggish, low pressure, venous beds.

4. Blood given intra-arterially may directly perfuse the coronary and cerebral vessels.

5. IAT may obviate the rise in central venous pressure and right heart failure that may result from rapid IVT.

6. Survival rate in experimental hemorrhagic shock is higher with IAT than with IVT.

The purpose, therefore, of the present experimental study has been to examine the rationale of IAT and to compare under rigidly controlled conditions the two routes of transfusion in the treatment of experimental hemorrhagic shock in dogs.

From the Department of Physiology, Naval Medical Field Research Laboratory, Camp Lejeune, North Carolina.

This work is not to be construed as necessarily reflecting the views of the Department of the Navy.

GENERAL METHODS

Sixty-four dogs were anesthetized with morphine tartrate (3 mgm. kgm. body weight) intramuscularly, followed in 30 minutes by a solution of chloralose (48 mgm. kgm.) and urethane (480 mgm. kgm.) intravenously. Paired litter mates of an inbred strain of beagle hounds were used in a few experiments to increase the rigidity of the experimental

control. Following anesthesia, the requisite number of arteries and veins in the extremities were exposed and cannulated for the measurement of pressures, and for the removal and reinfusion of blood. Animals used for survival studies were operated upon under sterile conditions and given prophylactic penicillin postoperatively. Central venous pressure was measured from a venous catheter, the tip of which was located in the right auricle. Arterial and venous pressures were measured with capacitance type pressure transducers. The zero reference point for all measurements of pressure heads was the skin of the back. Cardiac output was determined by the blue dye injection method employing a repeatedly calibrated photometer which continuously measured the dye concentration of flowing arterial blood. A lead II electrocardiogram was recorded during many experiments. Directional changes in the oxygen saturation of cerebral arterial and venous blood were obtained by continuously measuring the optical density of flowing blood to monochromatic light at 6,200 angstroms, a wave length at which oxygenated hemoglobin transmits more light than does reduced hemoglobin. Electric integration was used to obtain mean pressures.

Hemorrhage was accomplished by permitting the animals to bleed freely from an indwelling arterial needle into a suspended reservoir. Since the height of the reservoir determines arterial pressure, any degree of hypotension can be reached and maintained. Throughout, an effort was made to test the animals at all levels of circulatory embarrassment, including both reversible and so-called "irreversible" shock. The period of hypotension varied from 30 minutes to 4 hours. Intra-arterial and intravenous transfusions were administered by means of a calibrated hand operated pump; an electrically driven rotary pump; a syringe; or the standard pressure bottle infusion apparatus commonly used for IAT.

Pressures, arterial dye concentrations, electrocardiograms, and changes in oxygen saturation were recorded simultaneously on a direct writing multichannel recorder. Observations from 64 animals serve as the basis for the data reported. Data were analyzed statistically when indicated.

HYDRAULIC EFFECT OF INTRA-ARTERIAL TRANSFUSION

The rise of arterial pressure postulated to result from the direct hydraulic effect of the intra-arterial injection is the basic assumption on which the use of IAT rests. If IAT is superior to IVT, it may be because IAT produces an elevation of arterial pressure over and above the improvement that results from the restoration of blood volume and cardiac output which occurs after intravenous transfusion. Previous experiments (9) have demonstrated that the extent of the pressure rise created by IAT may be predicted by the Hagen-Poiseuille equation, provided that two factors are known: (a) the rate of the intra-arterial injection, and (b) the peripheral vascular resistance of the arterial system. According to the modified Hagen-Poisseuille equation,

$$\text{Rise in arterial pressure (mm.Hg)} = \text{Vascular resistance (arbitrary units)} \times \text{rate of IAT (ml./min.)}$$

Cournand and co-workers have determined the peripheral vascular resistance of a representative group of patients in hemorrhagic shock to be 0.0169 resistance unit. The average rate at which IAT is administered as determined from all reports in the literature in which transfusion rates are given is 22 milliliters per minute. The beneficial effect of IAT on arterial pressure can, therefore, be calculated to be 0.37 millimeter of mercury:

$$\text{Rise in arterial pressure} = 0.0169 \times 22 = 0.37 \text{ mm.Hg}$$

Confidence in the validity of this equation (Hagen-Poisseuille) is based on its application to the hydraulics of the circulation by physiologists for many years, as shown by Green. Extensive experimental study, observed elsewhere (13), provides further indication of the accuracy of this analysis.

An improvement in arterial pressure of less than ½ millimeter of mercury is hardly adequate to explain the favorable clinical results obtained with IAT. The mechanism by which IAT exerts its favorable effects must be sought elsewhere. It is also clear that the

pressure employed in the transfusion apparatus bears no direct relationship to the improvement in the patient's arterial pressure. The pressure of 100 to 200 millimeters of mercury commonly used in administering IAT is dissipated as energy loss in the tubing and arterial cannula; the hydraulic rise in arterial pressure is determined solely by the rate of blood flow through the intra-arterial needle, and by the peripheral vascular resistance of the patient.

Conclusion. The rise in arterial pressure attributable to the direct hydraulic effect of intra-arterial transfusion is insignificant because the rates of transfusion presently employed in clinical practice are so small. An explanation of the restoration of arterial pressure with IAT must be sought elsewhere than in its hydraulic effect.

RECOVERY OF ARTERIAL PRESSURE

The rationale for the use of IAT is to a large extent based on studies which demonstrate that the recovery of arterial pressure in dogs during hemorrhagic shock is more rapid with the arterial than with the venous route of transfusion. In such experiments, IVT was administered at approximately one-fourth the rate of IAT in order to avoid an acute rise in venous pressure, cardiac failure, and death, a sequence said to follow rapid IVT late in shock. The recovery of the animals receiving IAT was approximately 4 times as rapid as those receiving IVT. In the present studies, this experiment was repeated in 4 dogs. The results confirm the work of others in that recovery of arterial pressure is more rapid when the intra-arterial route of transfusion is used, as is illustrated in Figure 1. Although this type of experiment has been widely interpreted as demonstrating the superiority of IAT, Weiner has pointed out an alternate explanation which may be pertinent; the more rapid recovery of arterial pressure with IAT may be due to the more rapid rate of transfusion by the arterial route. Therefore, 3 additional series of experiments were done to compare the two routes of transfusion under comparable and controlled conditions.

Series A. Thirteen pairs of dogs, matched for weight and configuration, were studied 2

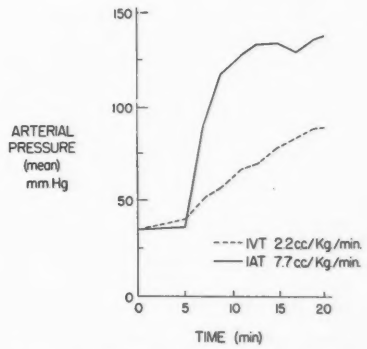


Fig. 1. Illustration presents the results of comparing slow IVT with rapid IAT. These are the mean values of 36 points from experiments on 4 dogs. The faster IAT effects a more rapid recovery of arterial pressure than does slower IVT.

at a time on the same operating table with identical recording systems. Each pair of animals was simultaneously bled to the same level of hypotension (25 to 60 mm. Hg) and maintained there for the same period of time (36 to 278 minutes). The amount of blood shed during that time varied from 3.1 to 6.4 per cent of body weight. At the end of the period of hypotension, all of the blood removed was reinfused at the same rate and by the same means employing the intra-arterial route in 1 animal, the intravenous route in the other. To prevent the involuntary introduction of bias by the investigators, the animal to receive IAT was determined by the toss of a coin 15 seconds before the simultaneous reinfusions began. The average rate of recovery of arterial pressure is the same for arterially and venously transfused animals (Fig. 2). Equal volumes of blood were equivalent in their ability to restore arterial pressure, regardless of the route of transfusion. Recovery appears to be a function, not of the route of transfusion, but of the rate of restoration of blood volume.

Series B. A dog was bled to an arterial pressure of 30 millimeters of mercury and then a portion of the blood removed was reinfused by the intra-arterial or intravenous route. Following recovery, the animal was bled to the same level and the same volume of blood was reinfused at the same rate by the

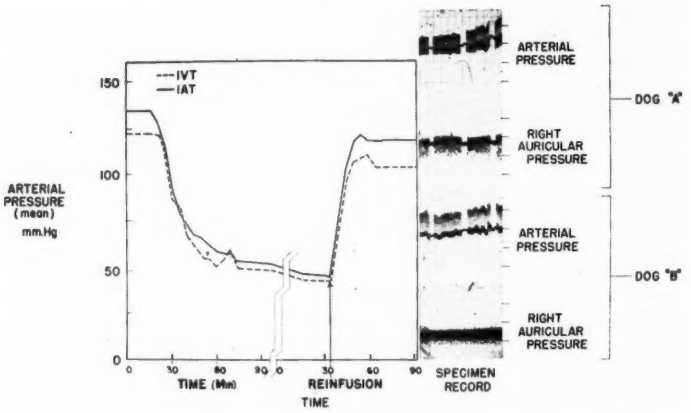


Fig. 2. Recovery of arterial pressure with IVT and IAT is illustrated by this replot of 418 points from experiments on 19 dogs surviving the acute experiment. There is no statistically significant difference in the recovery rate of arterial pressure when shed blood is reinfused at the same rate by the arterial and venous routes. The record at the right is representative of those from which these data were obtained. Interruptions in full pulse contour are electrically integrated mean pressures. The period of hypotension varies from ½ to 4 hours.

alternate route. This procedure was repeated 10 times in 5 dogs. The average rate of recovery of blood pressure is the same for IAT and IVT. Results are so like those of series A that no graphic presentation is warranted.

Series C. Ten animals were bled to shock levels. Reinfusion of all of the blood removed was begun at a rate averaging 1.3 milliliters per kilogram per minute (equivalent to 91 ml./min. in 70 kgm. man) by either the intra-arterial or intravenous route. At the end of a 4 minute period, the infusion was changed to the alternate route but continued at the same rate. Arterial pressure was measured continuously until all the blood had been reinfused. Alternate periods of IAT and IVT at the same rate are equally effective and produce the same increments in arterial pressure (Fig. 3). The validity of this method of detecting differences in effectiveness of transfusion is demonstrated by 4 control experiments in which IVT was given at 4 times the rate of IAT (2.0 ml. vs. 0.5 ml./kgm./min.). Figure 3 (inset) shows that the more rapid rate of transfusion produces a more rapid increment of arterial pressure.

Comment. Alrich and Morton have compared IAT and IVT at equal rates of infusion. These investigators were unable to demonstrate any superiority of IAT in bringing about recovery from hemorrhagic shock. The present experiments confirm this earlier work.

Conclusion. Under the conditions described, intra-arterial and intravenous transfusion are equally effective in treating the hypotension of experimental hemorrhagic shock.

RECOVERY OF CARDIAC OUTPUT

Hemorrhagic shock is a syndrome characterized by low cardiac output. A comparison of the effectiveness of the two routes of transfusion in restoring cardiac output, therefore, is a logical and heretofore unexplored avenue for investigation. Cardiac output was measured at 4 minute intervals during alternate periods of IVT and IAT as described in series C. Figure 4 presents the mean values for 84 cardiac output determinations on 8 dogs. It illustrates that there is no difference in the rate of recovery of cardiac output during periods of IVT and IAT. Control experiments (Fig. 4, inset) demonstrate the validity of this method of testing the effectiveness of two methods of transfusion. More rapid restoration of blood volume produces more rapid recovery of cardiac output.

Conclusion. Under the conditions described, intravenous and intra-arterial transfusion are equally effective in restoring the low cardiac output characteristic of hemorrhagic shock.

VENOUS POOLING

The effectiveness of IAT in rapidly restoring the circulation of the shocked subject to normal has also been attributed to the immediate participation of arterially injected blood in active circulation, whereas intravenously injected blood is said to remain pooled in sluggish, low pressure, venous beds. This hypothesis was tested by tagging with Evans blue dye the albumin fraction of the plasma of venously and arterially transfused blood prior to its administration. A continuous photometric analysis of the dye concentration in the general circulation could thus be used to determine the rapidity with which the transfused blood mixed with the circulating blood volume. Mixing of the transfused blood was compared to mixing of a standard dose of dye delivered into the right heart. Detailed description of the experimental method and analysis of the data are reported elsewhere (8). Within 90 seconds following tagged IVT, approximately 100 per cent of the injected blood may be accounted for in the general circulation as compared to the standard injection; under the same conditions, approximately 100 per cent of intra-arterially injected tagged blood may also be accounted for.

Conclusion. Compared with a standard technique, the mixing of transfused blood (plasma fraction) with the general circulation 90 seconds after injection is not significantly different following intravenous and intra-arterial transfusion.

VENOUS CONGESTION AND HEART FAILURE

The fear that rapid IVT may bring about venous congestion, heart failure, and death is frequently cited as a point in favor of transfusion by the intra-arterial route. As pointed out by Alrich and Morton, the evidence on this point has been obtained under experimental conditions which were not comparable for the two routes of transfusion. The following experiments examine the effect of IVT and IAT on central venous pressure when the transfusions are given at comparable rates. Continuous recordings of central venous pressure (right auricle) were made in 26 animals, studied simultaneously in pairs (series A) before induction of, during, and after recovery from hemorrhagic shock. Nineteen of the 26 animals survived the acute reinfusion of all blood removed following periods of hypotension (25 to 60 mm. Hg) lasting from 36 to 234 minutes. Fifteen survived indefinitely.

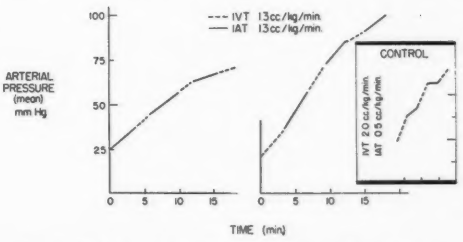


Fig. 3. This figure is a replot of 324 points from 17 experiments, and compares the recovery of arterial pressure with alternating periods of IVT and IAT. Alternating the route of transfusion does not affect recovery of arterial pressure. The two graphs illustrate that the initial route of transfusion employed has no effect. The inset shows the ability of the method to detect differences in the effectiveness of transfusion at different rates (note "stepladder" effect).

The average central venous pressures for all surviving animals are plotted in Figure 5.

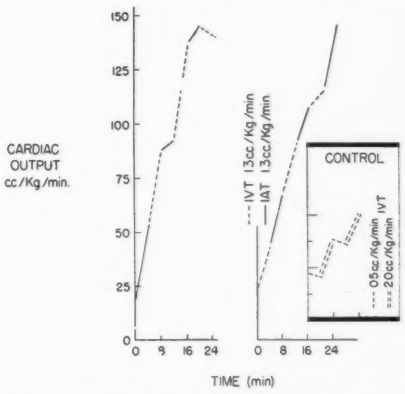


Fig. 4. The mean values of 84 cardiac output measurements from 13 experiments in 8 dogs are presented in this graph. Alternating the route of transfusion from IVT to IAT does not significantly affect recovery of cardiac output. The 2 charts illustrate that the initial route employed has no effect. The inset shows the ability of the method to detect differences in the effectiveness of transfusion at different rates (note "stepladder" effect).

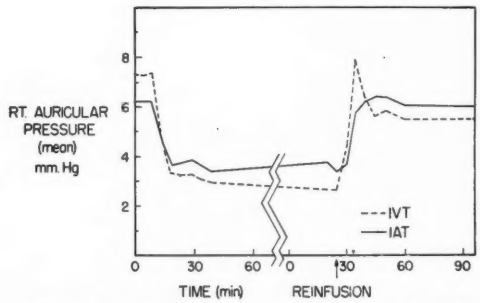


Fig. 5. Changes in central venous pressure with IVT and IAT are illustrated in this replot of 418 points from studies on 19 dogs surviving the acute experiment. There is no statistically significant difference in central venous pressure during recovery with IVT and IAT. The period of hypotension varies from ½ to 4 hours.

Central venous pressure falls sharply when hemorrhage is begun and remains low during the period of hypotension. When transfusion is given either intravenously or intra-arterially, central venous pressure rises to a value which is slightly higher than the control pressure of the animal but within 5 minutes returns to the prehemorrhage level. The venous pressure curves for the intravenously transfused animals are indistinguishable from those of the animals transfused intra-arterially.

Comment. The preceding experiments confirm earlier observations that the venous pressure of animals in hemorrhagic shock rises sharply (to normal or slightly above in these experiments) following the reinfusion of blood. The experiments add to previous observations by indicating that the rise is similar regardless of the route of transfusion employed, and are in agreement with the results of Alrich and Morton.

Seven animals succumbed during the acute phase of these experiments. If, at the time of transfusion, mean blood pressure continues to fall, pulse pressure becomes less than 8 millimeters of mercury, bradycardia occurs and peripheral arterial pulse contour becomes rounded, the prognosis is extremely poor. Reinfusion of blood at this time, whether by the arterial or venous route, was accompanied by an acute rise in venous pressure, asystole, and finally death by ventricular fibrillation. Changes in venous pressure during IVT and IAT in this group of animals are similar (Fig. 6). The final venous pressures are well above prehemorrhage levels. Transfusion cannot be said to be the initiating cause of the rise of venous pressure and death in these dogs, since the venous pressure of the animals which were not transfused followed a similar course. The acute rise in venous pressure was further demonstrated to be a nonspecific effect in 1 animal by duplicating the elevation in venous pressure and death by the intravenous injection of magnesium sulfate (Fig. 6, inset).

The acute rise of venous pressure in these experiments is a well recognized part of the pattern of death. With the diminution in effectiveness of cardiac activity, the high and low pressure sides of the circulation come into pressure equilibrium. The classical observation that blood shifts to the venous side of the circulation at the time of death is the explanation for the marked rise in central venous pressure. Infusion of a large volume of blood by either the arterial or venous route may result in the establishment of the equilibrium pressure at a slightly higher level, but the route of transfusion cannot be assigned a causative role in the death of the animal.

The recent experiments of Beattie and associates and Pierce and associates demonstrate that more than 130 per cent of the volume of hemorrhage must be rapidly injected into dogs in hemorrhagic shock in order that the infusion itself be the cause of death.

Conclusion. The rise in central venous pressure and the occurrence of "heart failure" in these experiments are unrelated to the route of transfusion employed.

SURVIVAL EXPERIMENTS

After the observations described were made, the 26 paired animals (series A) were followed to determine survival rate. It might be stressed that the animals were paired for weight and configuration and were studied simultaneously under rigidly controlled conditions. The route of transfusion for the individual animal was chosen by toss of a coin. The two methods of transfusion could be compared at all levels of shock, since each pair of dogs served as its own control.

Of 13 animals receiving IVT, 7 survived; of 13 treated by IAT, 8 survived. The study was

not extended to include more than 26 animals, since the physiologic data (8) obtained during the experiments gave no indication of a significant difference between IVT and IAT.

Conclusion. It was not possible under the described experimental conditions to demonstrate a significant difference in survival from hemorrhagic shock following intra-arterial or intravenous transfusion.

CEREBRAL AND CORONARY PERFUSION

The postulate that IAT brings about an increased perfusion of the cerebral and coronary vessels in hemorrhagic shock is of major importance to the rationale of this therapy. The following experiments evaluate the effect of IAT on cerebral and coronary blood flow. The theoretic viewpoint is also discussed.

Thirty-five per cent skiodan solution was injected into various parts of the arterial tree at rates varying from 200 to 400 millimeters per minute (volume 10 to 25 ml.). Distribution of this radiopaque material was followed with roentgenograms taken during or immediately after the injection. The circulatory condition of the animal varied from mild shock to the agonal state.

It was readily possible to demonstrate the skiodan filling the carotid arteries (Fig. 7a). It was noted that the deeper the level of hemorrhagic shock, the more retrograde the skiodan could be forced into the arterial tree. Increasing the rate of skiodan infusion also resulted in increased retrograde spread of the injected material. While cerebral perfusion was easily demonstrated, filling of the coronary arteries did not occur on repeated attempts even though mean arterial pressure was continually lowered. Not until blood flow from the left ventricle had been completely eliminated by precipitating ventricular fibrillation by the intravascular injection of ether, could skiodan be forced into the coronary arteries. Immediately after fibrillation appeared on the electrocardiogram, the skiodan injection was repeated in the same manner as previously performed. Filling of the coronary circulation was then demonstrable by roentgenogram (Fig. 7b).

Comment. These observations were repeated on a hydraulic model in which flow

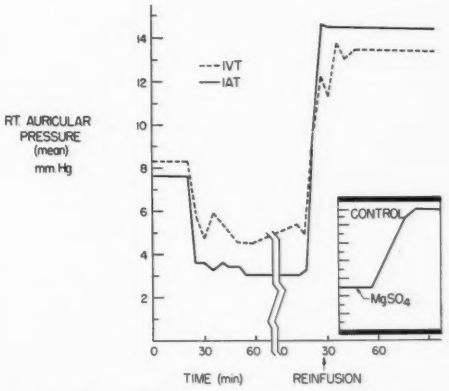
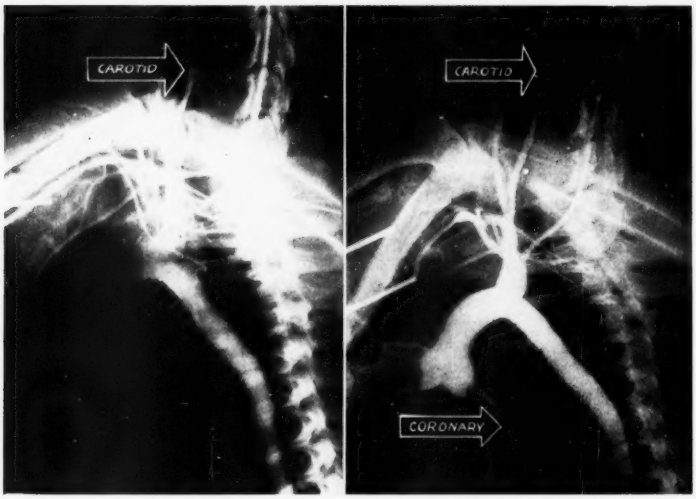


Fig. 6. This figure shows the changes in central venous pressure during death by "heart failure" following IVT and IAT (mean values of 168 points from experiments on 7 dogs which died during the acute experiment). IVT and IAT are accompanied by parallel rises of venous pressure in those animals which die acutely. That this rise in venous pressure is a nonspecific part of the agonal state is illustrated in the inset. Death induced by intravascular magnesium sulfate is accompanied by a similar rise. The period of hypotension varies from ½ to 4 hours.

rates, resistances, and rates of dye injection could be controlled. Both the animal and hydraulic model experiments are no more than a crude demonstration of the well known hydraulic equations which govern the distribution of blood within the arterial tree. It is predictable from available data that infused blood will not itself perfuse the coronary circuit until the rate of intra-arterial transfusion exceeds by 20 times[1] the cardiac output passing through the aortic valves. Such is the case since the hydraulic resistance of the peripheral vascular bed is about one-twentieth of that of the coronary circuit. To cause the arterially transfused blood itself to perfuse the coronary arteries of the patients in shock described by Cournand and associates (average cardiac output 3.80 L./min.), a representative series, would require in theory the inordinate infusion rate of 76 liters (152 bottles) per minute. Calculation from the same hydraulic equations indicate that perfusion of the cerebral vessels is somewhat more easily accomplished as the result of their lower vascular resistance and

[1]This ratio may be reduced in hemorrhagic shock due to compensatory changes in vascular resistance which tend to maintain coronary flow despite low total systemic blood flow.



a b

Fig. 7. a, Injection of skiodan into the brachial artery fills the descending aorta and carotid arteries of animal in shock but fails to appear in the coronary arteries. Hydraulic factors are discussed in the text. b, The coronary arteries are filled with skiodan in the absence of cardiac output during ventricular fibrillation.

more favorable anatomic relationship to the point of arterial injection.

Even should direct cerebral perfusion occur with IAT, it has not yet been demonstrated that such perfusion would be beneficial. Since stored bank blood ordinarily has a low oxygen content, it is conceivable that cerebral oxygenation might be reduced by such a procedure. The effect on cerebral oxygenation of intra-arterial injection of venous blood was, therefore, studied.

A dog was anesthetized and bled into hemorrhagic shock. Directional changes in cerebral arterial and venous oxygen saturation were obtained by passing a sample of carotid arterial or jugular venous blood continuously through the directional oximeter previously described. Venous blood to simulate stored bank blood was obtained from the same animal immediately prior to transfusion. IAT was then carried out via the right brachial artery at a sufficient rate (equivalent to 3,000 ml./min. in a 70 kgm. man) to cause retrograde perfusion of both carotid arteries.

Figure 8 shows that during such an infusion there is a decrease in both cerebral arterial and cerebral venous oxygen saturation. In the presence of such decrements, the mean partial pressure of oxygen in the cerebral capillaries must be reduced. This is an undesired consequence in view of the tissue hypoxia that already exists as the result of the hemorrhagic shock.

Comment. It is perhaps fortunate that the coronary circulation, by virtue of its high vascular resistance and anatomic position, is protected against direct perfusion by unoxygenated blood. The average rate of IAT reported in the literature (22 ml./min.) is undoubtedly less than the blood flow to the extremity into which the transfusion is administered. Hydraulic considerations indicate that the blood can flow retrogradely only as far as the first major arterial branches before being carried to the venous system. It is, therefore, unlikely that the brain is perfused with unsaturated bank blood in clinical practice.

The question of whether IAT results in any benefit to the coronary circulation resolves itself, therefore, into determining if the arterially injected blood displaces a column of oxygenated blood already present in the arterial tree and moves it through the coronary vessels. This problem can be answered on the

basis of already available data. In a given state of coronary vasoconstriction, coronary flow is a direct function of mean arterial pressure. It has been shown in the foregoing that the average increase in arterial pressure resulting from the hydraulic effect of IAT calculated from published data is about 0.37 millimeter of mercury. Even if the mean coronary arterial pressure of patients in hemorrhagic shock were as low as 50 millimeters of mercury then improvement in coronary flow will be about 0.37 part in 50, or about 1 per cent.[1] Such a minuscule change in coronary flow is immeasurable by present techniques and probably insignificant physiologically.

The effect of IAT on directly measured coronary flow has been studied by Case, Sarnoff, Waithe, and Sarnoff (4). These investigators were unable to find special advantage to the arterial route of transfusion insofar as the coronary circulation is concerned.

Conclusion. Direct perfusion of the coronary vessels by arterially injected blood in the shocked individual having any appreciable cardiac output is a virtual impossibility with presently employed techniques of IAT. If such direct perfusion of the coronary and cerebral vessels with unsaturated bank blood were to occur, it would have adverse effects by reducing the partial pressure of oxygen in the coronary and cerebral capillaries. In view of the rates of intra-arterial transfusion which have been employed, it is unlikely that the favorable results reported should be ascribed to perfusion of either the coronary or cerebral vessels.

RESUSCITATION FROM ASYSTOLE

Once the output of blood from the left heart has ceased completely due to asystole or ventricular fibrillation, there is little possibility of blood infused venously reaching the arterial tree. Blood infused arterially will, on the other hand, result in some flow on the arterial side of the circulation. This is the situation wherein IAT has a major theoretic advantage over IVT.

A series of experiments was carried out to compare the effectiveness of IVT and IAT in restoring cardiac action. Extremely rapid transfusion by either route was successful in a certain number of cases, although the relative effectiveness of the two methods was not determined. IAT was at first assumed to initiate heartbeat by perfusion of the coronary arteries. However, suggestive evidence was obtained to indicate that IAT may be effective by virtue of the rise in venous pressure it produces.

[1]A similar figure can be arrived at independently by employing the data on coronary conductance given by Green.

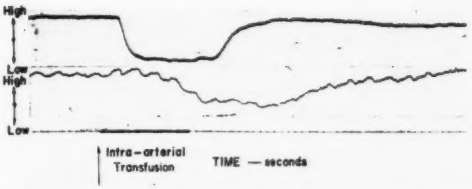


Fig. 8. A directional oximeter records changes in carotid arterial oxygen saturation (top channel) and jugular venous oxygen saturation (bottom channel) during IAT via the brachial artery. IAT with unsaturated blood results in a reduction in cerebral oxygenation.

Even should IAT be superior to IVT, IAT may be a poor choice of therapy when asystole occurs. The time required for setting up the apparatus and cutting down on the artery (e.g., 24 minutes in 1 case report) is a delay that may result in death. For this reason, Beck, in his discussion of the therapy of cardiac arrest, advises against the use of IAT.

DISCUSSION

This series of experiments once again demonstrates the effectiveness of restoration of blood volume as treatment for experimental hemorrhagic shock. The intravenous route was found adequate for this purpose; however it must be emphasized that IAT was also found to be an effective treatment for shock. In this respect, the present experiments fully confirm the scores of clinical reports which describe dramatic recoveries following the use of IAT.

Very rapid IVT has also been the subject of favorable reports. Pierce and associates describe the use of large IVT at rates which are faster than any that have been reported for arterial transfusion. Their results in treating shock are no less dramatic than those reported with IAT. Porter, Sanders, and Lockwood have had similar experience.

Data on the volume of blood administered by artery are given for 33 patients in 11 reports. In most cases the IAT was administered after the patient failed to respond favorably to IVT. These cases are repeatedly cited to indicate the effectiveness of the arterial route of transfusion in the treatment of shock. An analysis of the volume of blood administered reveals that the average patient had been given 1,700 milliliters intravenously before IAT was started. He was then given 1,685 milliliters intra-arterially, and so at the time of recovery of arterial pressure had received a total of 3,400 milliliters of blood. Thereafter, 1,480 milliliters were administered by vein. Thus, the average case citing the success of IAT has been given a total of 4,880 milliliters of blood, 35 per cent of it by artery. These figures serve to reaffirm the well established observation that the cornerstone of the treatment of hemorrhagic shock is the restoration of blood volume.

The experiments of Coles, described in a thesis submitted to the University of Western Ontario, are of interest. This investigator found abrupt changes in venomotor tone to occur with the trauma of arterial puncture. Whether such reflex alterations in vascular tone explain some of the results attributed to IAT is a matter of conjecture.

In addition to the recognized risks of blood transfusion, the infusion of blood intra-arterially under pressure is accompanied by the additional hazards of delay, ischemia, and necrosis of the extremity, extremity pain, and air embolism.

SUMMARY

A study of the relative effectiveness of intravenous and intra-arterial transfusion in the treatment of hemorrhagic shock has been carried out in a series of 64 dogs. Transfusions were administered by the two routes under comparable and rigidly controlled conditions. The experiments were so designed as to evaluate objectively the rationale which has been proposed to explain the favorable clinical results reported with the use of intra-arterial transfusion. The following observations were made:

1. The hydraulic effect of intra-arterial transfusion in elevating arterial pressure is insignificant at rates of transfusion which are presently employed clinically.

2. Recovery of arterial pressure is a function, not of the route, but of the rate of transfusion.

3. Intra-arterial and intravenous transfusion are equally effective in restoring the low cardiac output typical of hemorrhagic shock.

4. The rapidity with which intra-arterially and intravenously transfused blood mix with the general circulation was determined by a method in which the plasma fraction of the transfused blood was tagged. Compared to a standard technique, no evidence of pooling of the infused blood was found with either intra-arterial or intravenous transfusion.

5. Central venous pressure was found to fall during hemorrhage and to rise to normal or slightly above during reinfusion of previously shed blood. Changes in venous pressure and the occurrence of heart failure were unrelated to the route of transfusion.

6. Simultaneous, paired, survival experiments in 26 animals failed to show a significant difference in survival rate between intra-arterial and intravenous transfusion.

7. Direct perfusion of the coronary arteries by arterially infused blood was demonstrated by radiographic technique to occur only when the output of the left ventricle has become negligible or nonexistent. Direct perfusion of the cerebral vessels with unsaturated blood given intra-arterially was shown by directional oximetry to reduce both cerebral arterial and cerebral venous oxygen saturation.

8. In resuscitation from asystole, intra-arterial transfusion has some theoretic advantage over intravenous transfusion. In the present experiments, both methods of transfusion were found to be effective in restoring cardiac contraction. The relative effectiveness of the two methods was not determined. Intra-arterial infusion was assumed to initiate heart beat by perfusion of the coronary arteries. However, suggestive evidence was obtained to indicate that it may under some circumstances act via the venous system.

CONCLUSION

The rapid intravenous transfusion of blood has been demonstrated in these studies to be

an effective treatment for experimental hemorrhagic shock. No evidence could be found that rapid intra-arterial transfusion is any more or less effective.

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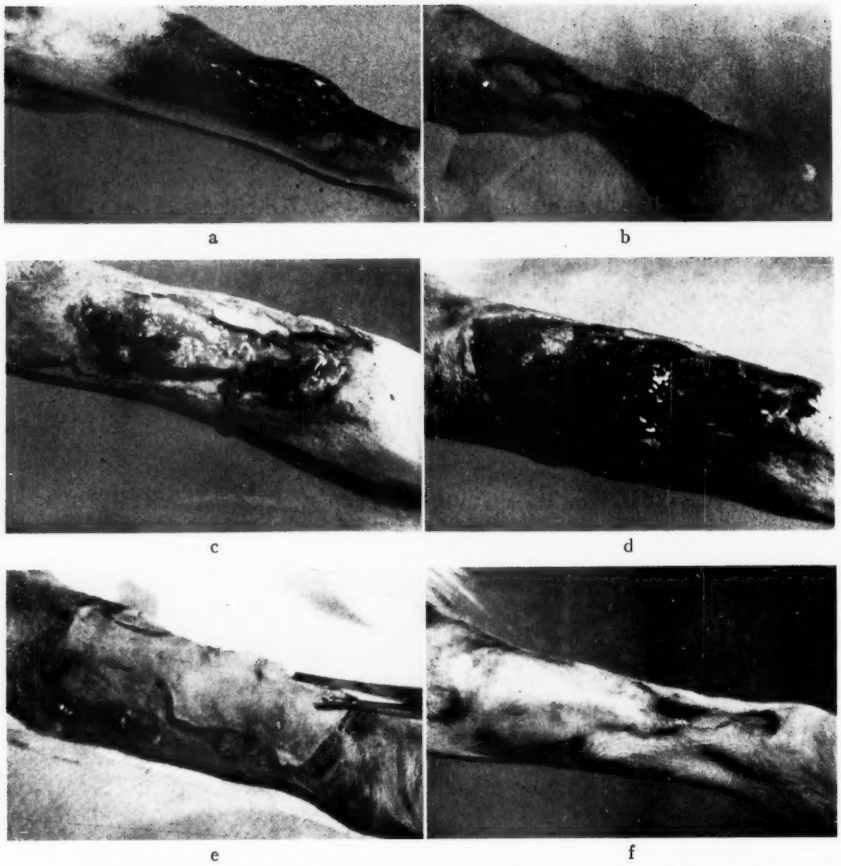

Fig. 5. Dog 9, series II. a, Foreleg immediately after open fracture of ulna and flame burn of wound and adjacent skin on December 9, 1952. Injury covered with dry compression dressing and leg immobilized with plaster. b, Appearance of wound 48 hours later following removal of the initial dressing. Excision of the wound to be performed. Dog started on parenteral penicillin. c, Foreleg 5 days after excision of the fracture wound and coverage of the fracture site with viable muscle. Whole thickness skin burn demarcated and ready for excision. d, Appearance of foreleg 2 days following skin excision and prior to application of partial thickness skin grafts. e, Partial thickness skin grafts on wound. f, Appearance of healed wound on March 24, 1953. Roentgenogram shows bone is united.

Experimental Study of the Treatment of Whole Thickness Burns Complicated by Open Fracture.—Harvey S. Allen, John L. Bell, and Sherman W. Day.

EXPERIMENTAL STUDY OF THE TREATMENT OF WHOLE THICKNESS BURNS COMPLICATED BY OPEN FRACTURE

HARVEY S. ALLEN, M.D., F.A.C.S., JOHN L. BELL, M.D., and SHERMAN W. DAY, M.D., Chicago, Illinois

THE problem of burns and fractures occurring at the same site in the human have been considered as a type of injury which could probably occur at the time of a civilian catastrophe. There is but little information in the literature which could be of aid in the management of such patients. Men of wide experience on the subject of extensive trauma have been consulted and the files at Cook County Hospital likewise have been searched and many men interrogated concerning their experience with this particular problem. Unfortunately, there is almost nothing to be gained from the experience of others on this combination of wounds; therefore, it was deemed best to carry this problem to the laboratory and to test whether the principles of management could be reproduced successfully on the dog. It is readily granted that a fracture and a burn on a dog are not the same as on a human, but we attempted to reproduce in miniature some of the basic factors concerned in this problem. We were concerned particularly with the fate of burned muscle in the presence of deep burning: how does bone appear that has been burned, and how will it heal?

Therefore, the ulna of the foreleg in one group and the fibula of the hind leg in another group were used to test the premise of soft tissue closure and fracture management in these dogs. Briefly, what we found could be transferred to surgery on humans, and it was noted that any lapse in surgical technique, i.e., inadequate excision or constant motion of the part, could result in a definite delay of healing. Basic principles of the treatment of trauma can be applied to a complex wound such as an open fracture and whole thickness burn, as any other large, open, contaminated injury.

A discussion of this combination of injuries has seldom been presented in the literature, and in recent years little interest has been shown in this problem. The early literature contains reports of isolated cases, usually the result of electrical burns with associated compound fractures. Each case was treated individually and there are no special techniques suggested. Warthin, in 1944, suggested an outline of care for fractures and burns. However, this report is not based on the conclusions which were arrived at by the end of World War II. Further, this report does not include management of shock, secondary closures of wounds, nor chemotherapy. There are several reports in the British literature, namely, Mansfield, Ross and Hulbert, Cohen, and Osborne, in the era of the last war, and again, not based on the final conclusions of the management gained from experience at the end of the last World War. Sir Watson Jones, in his recent book mentions this subject but briefly. The American literature, contains, notably, articles by Warthin, Bickel, Baldwin, Reynolds, and Kern writing of their experiences during World War II.

In the event of a catastrophe, large numbers of casualties having whole thickness burns and open fractures at the same level would be encountered. It seems that we sould have some basic rules to follow should we be confronted with a mass bombing attack. The first aid for such a complex wound could be easily handled with the use of previously prepared, large dressings which could protect the wound and fracture from further contamination and

From the Department of Surgery, Northwestern University Medical School, Chicago.

This work was supported (in part) by the Medical Research and Development Board, Office of the Surgeon General, Department of the Army, Contract No. DA-49-007-MD-495.

TABLE I.—TIMING OF EXPERIMENT IN SERIES I, IMMEDIATE EXCISION OF FRACTURE WOUND

	Days
Burn and fracture-wound excised	0
	1
Skin excision	2
	3
	4
	5
Skin grafting	6
	7
	8
	9
	10
	11
First dressing after graft	12
	13
	14

which would provide sufficient bulk to allow compression to be applied and a splint to be added. These large dressings, initially designed by our burn study group and approved by the National Research Council, have simplified the management of large, open wounds, whether the result of burns or other forms of trauma and have made it possible to dress an extremity or a trunk very satisfactorily within a matter of 2 or 3 minutes. These dressings not only serve adequately as first aid type of coverage, but also have a place in the management of later definitive care, particularly for large, raw, exposed areas following whole thickness burns, both before and after surgical excision and before and after skin grafting. Appropriate chemotherapy should be instituted immediately in a complex type of wound such as fractures and burns, and these drugs should be continued or altered as is necessary.

The shock state which would be produced by such an injury as whole thickness burn and open fracture would be difficult to manage. Initially, the open fracture, blood loss, and tissue damage would produce the typical picture of traumatic shock, and to this would be added burn shock, more prolonged in nature and more formidable to manage. It is imperative that the surgeon be aware of the fact that the burn shock would exist for about 48 hours and that during this interim, even after the initial wound shock has been combatted, the patient would demand observation. It would seem that the use of whole blood would be indicated for correction of the initial blood loss from the open fracture. After the first 24 hours, more accepted methods of burn shock therapy could be used. The surgeon not familiar with burns should be thoroughly informed on the necessity of correlating at appropriate intervals the general condition of the patient, fluid administration, and urinary output. Finally, oral therapy would probably be contraindicated, for many of these patients would be operated upon immediately under general anesthesia for excision of the fracture wound.

Ideally, the open fracture should have careful excision of all devitalized tissue, removal of foreign material, drainage of hematoma, and simple alignment of fracture, followed by coverage of the exposed fracture with adjacent viable soft tissue. The wound should be dressed with dry, fine mesh gauze and resilient compression with the intention of secondary closure being performed at a later date, preferably within 5 to 7 days. Burned wounds can seldom be assessed accurately at the time of the injury or immediately thereafter. Such wounds should be dressed and immobilized, and at the time of secondary closure of the open fracture, excision of the whole thickness loss of skin could be performed. Following this, in 48 to 72 hours, skin grafting of the wound could be undertaken. In other words, standard surgical procedures would be indicated.

Management of the fracture would be complicated, and it is impossible to conceive of a set of rules for immobilization which would apply to all fractures. Certainly the success of any open fracture management depends upon adequate excision of the wound itself and rapid healing of the soft tissue wound. Reduction of the fracture can be performed at the time of this excision, and maintenance of the position of the fracture would test the ingenuity of even the best trained orthopedic surgeon. Simple traction, plaster traction, skeletal traction, and even intramedullary pinning would have a place depending on the various types of fractures and their anatomic locations. The principles of absolute immobilization, asepsis, and early wound closure are too well known to be further emphasized at this time.

LABORATORY METHOD

Mongrel dogs, varying in weight between 13 and 20 pounds, were anesthetized with intravenous nembutal. The foreleg was clipped of hair and a longitudinal incision 4 to 7 centimeters in length was produced on the ulnar aspect of the leg. The ulna was exposed by blunt and sharp dissection and was fractured with bone-biting forceps. The proximal end of the fractured bone was displaced from the wound by inserting an instrument beneath the bone. The wound and the surrounding skin were then burned with the flame of a Bunsen burner until the skin contracted to a maximum and the periosteum of the proximal bone fragment turned black. Approximately 40 to 90 seconds were required to produce consistently a whole thickness burn of the skin adjacent to the open fracture. Sterile technique was not used for this procedure. Two series of dogs were prepared and in each series a group of animals received parenteral penicillin therapy in addition to the surgical procedures. The main variation in these two series was the time of the excision of the wound. In series I, immediate excision of the fracture-wound was performed, while in series II, the wound was covered only with sterile gauze and immobilized and then excised 48 hours later. The latter was done with the idea of attempting to simulate catastrophe conditions in which wound excision might well be delayed for at least this period of time. In each of the two series, either primary or delayed wound excision was performed and the wound eventually grafted.

DETAILS OF DRESSING AND IMMOBILIZATION

Because of the character of the wound and our belief that such a wound should demand a compression type dressing and immobilization, it might be of value to describe the dressing used on these animals, which is not different from the type which would be used for a human. Flat, dry gauze over the wound and a generous amount of fluffed dressings surrounded by sheet wadding provided a resilient dressing, and an elastic type of bandage completed the compression dressing. This dressing was comparable, at least in effect, to the type advocated for any wound necessitating evenly distributed compression. A plaster mold of 3 inch plaster of Paris was applied from above the elbow to the tips of the toes and was held in place by the use of a simple protective bandage. The dressings served satisfactorily for immobilizing the extremity and protecting the wound from the animal's natural desire to "lick" his wound. The usual superficial laboratory burn to the dog's leg will heal when exposed to constant licking by the animal.

TABLE II.—TIMING OF EXPERIMENT IN SERIES II, EXCISION OF FRACTURE WOUND 48 HOURS POST BURN

	Days
Burn and fracture	0
	1
Fracture wound débrided	2
	3
	4
	5
Skin burn excised	6
	7
	8
Skin graft	9
	10
	11
	12
	13
Dressing	14

In dogs receiving penicillin, the drug was started 48 hours after injury and continued until day of first dressing after grafting.

At no time have there been any ill effects from the use of such compression dressings with immobilization, as described. The use of plaster of Paris next to the wound itself would be hazardous and a method which is not to be utilized or condoned. To apply a nonresilient type of bandage as a complete encircling plaster cast over a burn or fracture site carries with it very definite hazards of pressure necrosis, not only compromising the skin but as has been seen clinically, involving nerves and vessels with great harm to the patient.

LATER CARE

In both series of dogs, whether excision was immediate or 48 hours later, an interval of 4 to 5 days was allowed before removal of the whole thickness burned skin was performed. Following that, 48 to 96 hours later, the clean wound of the burned site was grafted.

Dressings and plaster immobilization were discontinued after the soft tissues healed. The reparative process of the bone injury was

TABLE III.—SUMMARY OF SERIES I, IMMEDIATE EXCISION OF FRACTURE WOUND AND DELAYED EXCISION OF WHOLE THICKNESS SKIN LOSS

Dog No.	Date injury	Condition of graft at initial P.O. dressing	Result of wound healing	Result of fracture healing	Remarks
2	7–31–52	0% take. Removed its cast 2 days post graft	Healed spontaneously 14 weeks, 11–6–52	United—x-ray 4 months	1st dogs had difficulty keeping casts on
5	11–6–52	40% take	Healed spontaneously by 13 weeks, 2–10–53	United—x-ray 19 weeks	Graft resolved in 1st postgraft week
7	11–20–52	Not grafted. Mange	Healed spontaneously 13 weeks, 2–24–53	United—x-ray 17 weeks	Healed spontaneously. Not grafted because of mange
17 Penicillin	3–10–53	50% take. Dog removed cast at 6 days post graft	Healed by graft proliferation in 5 weeks, 4–10–53	Clinically solid, 6 weeks. United—x-ray 7–2–53	Removed its cast before 1st postgraft dressing could be done; 50% grafts were present, however
18 Penicillin	3–17–53	50% take	Healed by graft proliferation in 5 weeks, 4–21–53	United—x-rays 7–2–53	Removed its cast before 1st postgraft dressing; 50% grafts were present, however
19 Penicillin	3–31–53	90% take	Healed by graft proliferation in 4 weeks, 4–28–53	United—x-rays 7–2–53	Healed well
20 Penicillin	3–31–53	90–95% take	Healed by graft proliferation in 4 weeks, 4–28–53	United—x-rays 7–2–53	Healed well

observed by clinical and roentgenographic methods. It is recognized that this problem is not concerned with fractures alone, hence the problem of osseous healing was not closely investigated. The intact radius or tibia provided immobilization for the fractured bone. We were not concerned with the methods of immobilization of the fracture which, in the human, would vary with the site of the fracture and the condition of the patient. Our concern was mainly with management of the soft tissue injury and the healing of all components of the wound.

OBSERVATIONS ON CREATING BURN WOUND

After creating the wound and the fracture, the flame of the Bunsen burner was played over the incised wound and fractured bone and surrounding skin until sufficient burning was obtained to create a whole thickness type of burn. When the skin adjacent to the wound had contracted to a maximum and the exposed bone turned black, a deep burn occurred. It was most difficult to judge clinically what immediate damage the flame produced upon the muscle because the muscle and subcutaneous tissues exhibited an outpouring of red, watery fluid which seemed to bubble from the tissues. It was necessary to sponge away this secretion so that the exposed bone could be assessed when it had become blackened.

During and immediately following the burning, the blood which appeared from the depths of the wound turned black and there was a continuing of the thin, red, edema-like fluid pouring forth from the wound. The burned muscle was grayish-red in color and, if cut or pinched with a forceps, it neither bled nor contracted. The tendons appeared either yellowish-white, with definite fluid within the tendon itself, or grayish-white and dry. The burned skin which contracted under the direct impact of the flame was variable in color from a yellowish-gray to black, in contrast to the unburned skin. At this time it was difficult to assess accurately the area of skin burned, or to estimate accurately the exact depth of the skin burned.

Vesicle formation was not observed when this method of burning was used. By constant observation it was possible to produce a whole thickness skin burn consistently. In 48 hours, the burned skin could be easily distinguished from normal skin.

Dark-skinned dogs were, in general, harder to burn, for it took longer and it was most difficult to tell the depth of the skin burned immediately after the injury. Burns produced on light-skinned dogs, those brown, white, or black and white, were easier to evaluate immediately following the thermal injury.

TABLE IV.—SUMMARY OF SERIES II, EXCISION OF FRACTURE WOUND 48 HOURS POST BURN AND DELAYED EXCISION OF WHOLE THICKNESS SKIN LOSS

Dog No.	Date injury	Result of grafting at initial P.O. dressing	Result of wound healing	Result of fracture healing	Remarks
3	8–19–52	0% take	Healed spontaneously by 12 weeks, 11–6–52	X-ray—bone united at 7 months. Clinically solid, 14 weeks	Dog healed spontaneously
4	11–4–52	10% take	Healed spontaneously by 14 weeks, 2–14–53	X-ray—bone united at 4 months. Bone clinically solid, 14 weeks	Dog healed spontaneously
6	11–18–52	0% take	Healed spontaneously by 13 weeks, 2–24–53	X-ray—bone united at 17 weeks. Bone clinically solid, 13 weeks	Dog healed spontaneously
8 Penicillin	12–9–52	85–95% take	Healed by graft proliferation at 4 weeks, 1–6–53	X-ray—bone united at 15 weeks. Bone clinically solid, 6 weeks	Grafts proliferated; healing took place in 4 weeks
9 Penicillin	12–9–52	85–95% take	Healed by graft proliferation at 5 weeks, 1–13–53	X-rays—bone united at 15 weeks. Bone clinically solid, 6 weeks	Grafts proliferated; healing took place in 5 weeks
10 Penicillin	1–6–53	80–95% take	Healed by graft proliferation at 10 weeks, 3–17–53	X-ray union 7–2–53. Clinically solid, 10 weeks	Grafts proliferated; many of casts removed by dog delayed healing.
11 Penicillin	1–13–53	50% take	Healed by graft proliferation at 5 weeks, 2–17–53	X-ray union 7–2–53. Clinically solid, 10 weeks	Wound healing by graft proliferation
12 Penicillin	1–20–53	80% take	Healed by graft proliferation at 6 weeks, 3–3–53	X-ray union 7–2–53. Clinically solid, 9 weeks	Wound healing by graft proliferation
13 Penicillin	1–27–53	10% take. Removed cast 2 days post graft	Healed spontaneously in 7 weeks, 3–17–53	X-ray—bone union at 8 weeks	Removed cast 2 days post graft
16 Penicillin	3–3–53	50% take	Healed spontaneously by 4 weeks	X-ray union 7–2–53. Clinically solid, 6 weeks	Healed mostly spontaneously; most grafts lost after 1st dressing
21 Penicillin	2–24–53	50% take	Healed by graft proliferation at 7 weeks, 4–14–53	No x-rays. Clinically solid, 7 weeks	Healed. No x-rays

SURGICAL EXCISION OF THE OPEN FRACTURE

In order to follow surgical principles of wound management consistently, the fracture-wounds demanded careful and accurate surgical excision and debridement under anesthesia. In series I this was done immediately following injury, while in series II this maneuver was delayed for 48 hours. In each case, the wounds were prepared for surgical excision by using aseptic technique. Surgical excision was not particularly different from that which might be anticipated in a human. In each animal the obvious devitalized subcutaneous tissue, muscle, and tendons were excised to normal, bleeding structures. Blackened bone ends were not disturbed. The fractured sites were covered with adjacent soft tissues. There was minimal bleeding and only rarely was ligature of blood vessels required.

SURGICAL EXCISION OF WHOLE THICKNESS BURN LOSS

In both series, after the complex injury had been created and the resulting wound adequately excised, the wound was covered with a single layer of dry, fine mesh gauze and a compression dressing, and a splint was added. Two to 7 days later, the wounds were again observed, and at this time definite delineation of the whole thickness burned skin could be determined. With aseptic precautions this necrotic skin was surgically removed, as would be done on the human. At this time, the appearance of the fracture-wound, if excision had been adequate, was satisfactory. There were a few cases in which further excision of some devitalized muscle and tendon was required. Following surgical excision of the burned skin, the wound was dressed with a

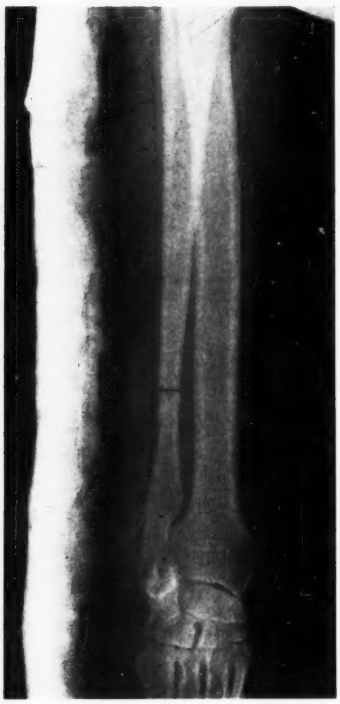

Fig. 1. Dog 18, series I. Roentgenogram of foreleg 7 days after fracture and flame burn. Plaster mold can be seen on ulnar aspect of foreleg. This dog was treated by immediate wound excision, delayed skin excision, and skin grafting 7 days following injury.

dry compression dressing and a splint was applied.

TECHNIQUE OF SKIN GRAFTING OF DOGS

Since it seemed imperative that the wounds created by the burning be of whole thickness character to create a genuine problem, it naturally followed that successful closure of these wounds should be performed. In these animals, the wounds varied from 4 by 8 centimeters to 12 by 8 centimeters and required closure by skin grafting. The dogs were anesthetized with intravenous nembutal, the hind leg and flank were shaved, and the skin was prepared with iodine and alcohol and dried with ether. Partial thickness skin grafts were taken freehand to provide sufficient skin for coverage of the wounds. The donor site was dressed with a light, protective dressing of sterile gauze. Donor sites were observed to close over rapidly and were healed within 7 to 10 days. However, the healing was not to the degree that a new graft could be taken from the same site for at least another week. After the donor skin was obtained, the dressing was removed from the injured extremity and the skin grafts were carefully spread over the open wound. The grafts were held in place by snubbing them into position by the aid of a compression dressing and splint which were not disturbed for from 5 to 7 days.

CONTROLS

These dogs were prepared in the same manner: an open fracture produced and the wound burned, but they were treated by dressings and immobilization only. No surgical excision was performed and no antibiotics were given. Dog 14 removed the dressing on the fourth day post burn, at which time the wound was grossly suppurative and the fracture site was exposed. There was no evidence of a spreading infection of the extremity.

Dog 15 was dressed in the usual manner, and 7 days post burn the wound was observed to be grossly suppurative. This wound was dressed at 2 to 5 day intervals, the suppuration persisted, and the fracture site remained exposed. The wound did not clean up until the necrotic tissue in the depths of the wound and the necrotic skin spontaneously sloughed away.

The history of these wounds on these 2 control animals is what one might expect when neglect of surgical excision has been allowed to occur.

RÉSUMÉ AND OBSERVATIONS ON SERIES I

Seven animals were prepared by creating an open fracture, burning, and subjection to immediate excision of the fracture-wound. Two to 5 days later, surgical excision of the burned skin was performed, and approximately 2 to 4 days following this skin grafting was undertaken. Four dogs received daily intramuscular penicillin injections from the time of the injury until the initial dressing following skin grafting of the wound, and 3 dogs received no antibiotics.

Excision of the burned muscle, fascia, tendon, and subcutaneous tissue was difficult technically because of the continuing wound secretion immediately following the burn. It was difficult to determine grossly which tissues had been burned to the point of devitalization. The viability of the tendon was difficult to determine at the time of immediate excision, and in most instances it was necessary to perform further excision of fascia and tendon at the time of the excision of the burned skin.

In the last 2 dogs, Nos. 19 and 20, the skin burn was ignored at the time burned muscle and fascia were excised, and the wound edges were approximated loosely, even though this entailed suturing through burned skin. Forty-eight hours later, the wounds were dry and the burned skin was demarcated sufficiently to permit surgical excision. The grafts applied to the wounds in all the dogs of series I did not vary greatly in their healing from that which might be anticipated in a similar series of humans. Excision of the wounds created in these experiments might have been easier to perform if a blood pressure cuff had been applied prior to the surgical excision to prevent constant oozing from the wound.

In 3 dogs of this series in which no antibiotic was used, the wounds at the time of the change of the initial dressing after excision revealed no suppuration. The legs were not swollen, except in 1 instance in which plaster and tape above the elbow had been applied too tightly. The wounds appeared clinically clean, but the results of skin grafting in these 3 dogs were not satisfactory. Although the take of the skin grafts was poor, the wounds continued to appear clean clinically, and epithelization of the wounds occurred by ingrowth from the periphery.

In the remaining 4 dogs of series I, intramuscular penicillin was started on the day of the injury and was continued until the first dressing was changed following skin grafting. In these dogs, the wounds at the time of skin grafting were clean with no gross suppuration nor edema. The results of skin grafting were uniformly more satisfactory. The final results revealed good healing of the soft tissues and solid union of the fractured bone.

Fig. 2. Dog 8, series II. Roentgenogram of foreleg with union of ulna on March 24, 1953. Treatment by delayed surgical excision, skin grafting, and parenteral penicillin.

RÉSUMÉ AND OBSERVATIONS ON SERIES II

In this group of animals, an attempt was made to simulate conditions which might be encountered after a catastrophe. Following the experimental injury to these animals, the wounded extremity was covered by a sterile compression dressing and plaster splint for the first 48 hours. After change of the dressing at 48 hours, the fracture-wound was excised, the bone ends aligned, and the fracture site covered with normal appearing tissue. Four to 5 days later, the necrotic skin was excised, and 2 days later, skin grafts were applied to the wounds. Four animals in series II received no antibiotics. Eight dogs were given penicillin by daily intramuscular injections of 300,000 units, starting at the time of surgical excision of the wound. This antibiotic was continued until the first change of dressing after the skin grafting.

Fig. 3. Dog 4, series II. Roentgenogram of foreleg on March 24, 1953, showing union of fracture sustained on November 4, 1952. This dog received no antibiotics. The fracture wound was excised 48 hours post injury followed by later excision of necrotic skin and application of skin grafts. Skin grafts did not take well and the wound healed from the periphery.

At 48 hours post burn, the initial observation of these wounds revealed no gross suppuration nor signs of spreading infection. The level of the burned wound was depressed about 1 millimeter from the surrounding skin, and there was a moderate serous outflow from the fracture-wound. The whole thickness skin burn was grayish-white or yellowish-white and was softer to touch than normal skin. The surrounding areola of partial thickness skin loss was usually not more than 2 or 3 millimeters wide, pink in color, and not as soft as the whole thickness burn. Other burned soft tissue was grayish-white or grayish-red and thrombosed vessels were prevalent. The wound was often covered with coagulated blood, which was black and could be easily wiped away without causing bleeding. The involved muscle was soft and could not be handled by tissue forceps without causing it to fracture or shred away. At this time, the difference between viable and nonviable muscle was readily apparent. It was difficult to determine the viability of tendons except those which were definitely charred or partially liquefied. A blood clot was usually present between the ends of the fractured bone.

In 3 dogs an attempt was made to reduce the size of the excised wound by undercutting the subcutaneous tissues and approximating healthy appearing subcutaneous tissue or fascia. This could be done only when adequate excision of devitalized underlying structures had been performed.

The excision of the burned skin in this series was not remarkable, for there was sufficient delay between burning and removal of nonviable skin to allow for satisfactory demarcation. Excision of the burned muscle, tendon, and fascia was facilitated by including a 2 or 3 millimeter margin of burned skin and dissecting from the periphery into the depths of the wound.

In 1 dog, No. 16, the wound and the surrounding necrotic skin were excised at one stage. This was a black dog, and the area of skin involved by the whole thickness burn proved to be much less than was anticipated. In this instance, grafting was performed 3 days later with a fair result. In none of the dogs was there a problem of gross infection or swelling of the leg.

In 4 dogs not receiving parenteral penicillin, although the wounds appeared surgically clean at all phases, the result of skin grafting was poor. One animal was not grafted because of distemper. Cultures of this series were taken at the time of wound excision, at the time of skin excision, and before the grafts were applied, and showed growths of nonhemolytic and hemolytic streptococcus and nonhemolytic staphylococcus.

In the 8 dogs which received penicillin the wounds appeared surgically clean at the time of skin grafting, and there was à very excellent take of the skin grafts. Complete healing of the wounds was obtained. In 2 of the dogs

further excision of muscle was required before the skin grafts were applied.

MORTALITY OF THE DOGS

There were 2 dogs which were sacrificed: dog 1 of series II, because of distemper, 14 days after injury, and dog 14, a control, which was sacrificed 4 days after injury because his dressing and splint had been removed and the wound was grossly suppurated with the fracture site exposed. None of the dogs died from spreading infection.

CONCLUSIONS IN TREATMENT OF FRACTURES AND BURNS ON DOGS

It is natural that in handling animals there was variation in individual response, and, as in treating humans, it is difficult to maintain constantly satisfactory dressings and prevent movement of the extremity. In some animals, as in some children, this was no problem, while in others, it was a constant problem and, in many instances, contributed to an alteration of the wound healing.

Primary excision of the fracture-wound at the time of injury was not simple to perform. It was definitely easier to accomplish a cleaner wound débridement in dogs of series II because recognition of the obviously devitalized structures was facilitated by the delayed excision. At 48 hours the tissues were dry and were accompanied by less oozing of serum.

It is possible that the burn of muscle and tendon is not particularly different from the burn of skin in that initially the exudation of tissue fluid makes it most difficult to determine the exact extent of the injury. It is questionable whether this conclusion can be applied to a wound of the same type in a human. However, it was of interest to note that these wounds in dogs did not show gross suppuration within 48 hours, if they were simply protected. This in no way should be construed as a recommendation, contrary to known and proved surgical principles, for delaying wound excision in any case. It will demand clinical experience by well trained observers to arrive at such a departure from accepted treatment.

The factor of crushing of the tissues inflicted with the burn was not studied in this experiment. It is well known that crushed wounds heal much differently from others, and certainly this particular group of animals were not subjected to sufficient crushing to allow them to be compared to another in which the factor of tearing, crushing, and contusion has occurred.

Fig. 4. Dog 11, series II. Roentgenogram of foreleg on March 24, 1953, showing lack of bony union although wound was well healed and skin grafts had taken. Bone was clinically solid at this date. This animal received intramuscular penicillin, starting 2 days after the injury on January 13, 1953.

In the dogs, as in humans, failure of wounds to close well could be attributed to omissions of surgical principles. The wounds did not heal well when complete and satisfactory excision had not been performed, and, similarly, when complete immobilization was not carried out.

A wound of a dog's skin has a great tendency to epithelialize from the undamaged edges. This phenomenon will occur more rapidly in a dog than a comparable defect in a human.

The wounds of these animals demonstrate again that contamination of the open wounds does not necessarily mean spreading infection, for contamination of these wounds was obviously present. The bacterial flora which was encountered was of the type which was susceptible to systemic penicillin therapy. There was a definite improvement in the take of the skin grafts on dogs which were covered by penicillin.

Compression dressings, as described, if properly applied to the dog's extremities, do not provoke swelling of the extremity, ulceration of the extremity, nor infection of the extremity.

Although the problem of bone healing in these two series of animals was not checked microscopically, it was confirmed by clinical and x-ray evidence. However, the fractures may not have been realistically produced since the presence of the intact radius provided adequate immobilization at the fracture site.

COMMENT

To relate this study to human burns and injuries of a similar nature, while not valid in all respects, is undoubtedly possible, for here, as in the human, it was shown that early closure is desirable and feasible. Good surgical care will determine the outcome. Good surgical care demands: asepsis; accurate removal of devitalized tissue; rest; compression to diminish posttraumatic edema; and a rapid conversion of the open, contaminated wound to a clean, closed wound.

Because of the paucity of information in the literature, it is hoped that this study may stimulate others to think of this problem and to concentrate on methods of immobilizing and maintaining reduction of various fractures of the human body during the time that the burned wound is being closed. The objective in all wound surgery is to accomplish wound closure as quickly as is possible and practical, and to stage the wound closure as conditions dictate.

We believe that in the presence of mass casualties the simple, but proved, surgical principles of wound management are indicated. At such a time basic methods should be followed.

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THE TREATMENT OF FRACTURES COMPLICATED BY CONTIGUOUS BURNS

An Experimental Study in Dogs

WILLIAM T. FITTS, JR., M.D., F.A.C.S., BROOKE ROBERTS, M.D., WILLIAM J. GRIPPE, M.D., MARK W. MUIR, M.D., and MARK W. ALLAM, V.M.D., Philadelphia, Pennsylvania

AN ERA of atomic warfare should bring a large number of casualties consisting of fractures complicated by contiguous burns. In the event of mass bombing attacks, a considerable number of severe "fracture-burn" problems would have to be cared for rapidly and should be cared for according to some previously tested plan. To our knowledge no such plan has yet been proposed.

The ideal method for treating these combined injuries is a method which is optimal for treating the fracture and which allows, at the same time, complete freedom in treating the burn. An accepted form of treatment for certain fractures of long bones is fixation with an intramedullary nail. Intramedullary nailing might be the best method available for the treatment of certain fractures complicated by contiguous burns. Its chief advantage, as far as care of the burn is concerned is that it eliminates external fixation and leaves the burned area free to be treated in any desired manner. The question arises whether this advantage is outweighed by the increased risk of infection resulting from nailing in the presence of an open wound. Does the nailing operation, performed through burned skin and leaving a foreign body in the medullary canal, predispose to serious infection and delayed healing of either bone or skin, or does the rigid fixation afforded by the nail outweigh the increased contamination of the fracture site and the burn, as well as the presence of a foreign body in the medullary canal? Doubtless, an operation performed through a contaminated wound increases the risk of bone infection, but so does motion at the fracture site. The rigid immobilization obtained by intramedullary nailing may so decrease the risk of active infection that it more than compensates for the operative contamination and the presence of a metallic foreign body. A great advantage of intramedullary nailing over skeletal traction for these injuries is that it allows complete freedom in moving the patient, and, therefore, makes early evacuation possible. It also allows early ambulation in most instances.

We have approached this problem by experiments with fractures of the radius and ulna of dogs—both open and closed—complicated by contiguous burns produced by immersion in hot water. A fracturing appartus was devised for the production of closed fractures of both the radius and ulna, similar on the two sides. Open fractures were produced by fracturing the ulna alone at approximately the junction of the middle and distal thirds with a Gigli saw. The ulna, if fractured alone at this level, is well stabilized by the intact radius and unites without added stabilization. An intramedullary nail adds a slight degree of fixation. If both the radius and ulna are fractured some method of immobilization is essential to allow good healing. If the fractured radius is fixed with an intramedullary nail, the ulna is sufficiently stabilized so that healing of both bones will occur promptly without added fixation. In these experiments we compared intramedullary nailing on one side with treatment by plaster of paris immobilization of the opposite leg. The only difference between the two sides was in the method of treatment. Because each dog served as its own control, all systemic factors

From the Harrison Department of Surgical Research, School of Medicine, University of Pennsylvania and the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.

This investigation was supported by Contract No. DA-49-007-MD-253 between the Department of the Army and the University of Pennsylvania.

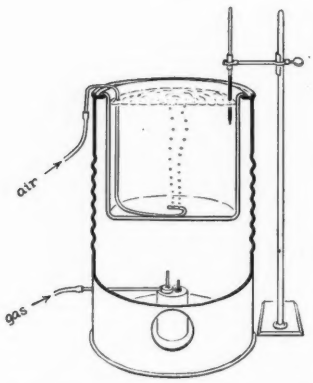


Fig. 1. Apparatus used for burning foreleg between elbow and paw. Water kept at temperature of 90 degrees C.

which might alter fracture healing—e.g., age, sex, nutrition, and activity—were eliminated.

REVIEW OF LITERATURE

A review of the literature indicates that little has been written about this potentially important aspect of trauma. An annotated bibliography compiled by Baer for the Armed Forces Medical Library on Pathology and Physiology of Burns, in 1942 to 1951, gives only 3 references concerning bones or cartilages as affected by burns (5, 7, 9), and these

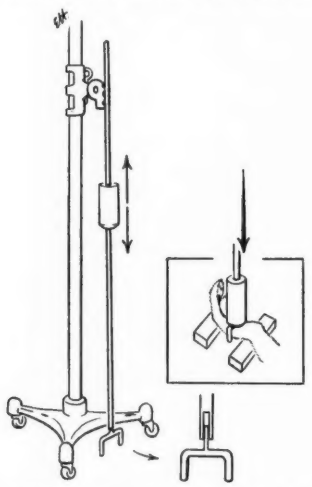


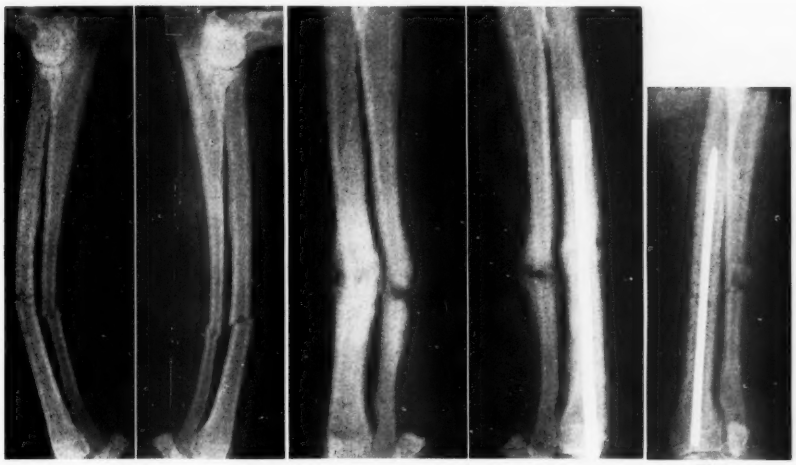
Fig. 2. Fracturing apparatus used for producing closed fractures of both radius and ulna of the dog.

are not concerned with fractures and burns, but with osteoporosis and perichondritis following burns. Most writers have advocated closed plaster treatment for fractures with contiguous burns except for fractures of the femur, for which they advised skeletal traction. The claim was not made that the best treatment for the fracture could always be associated with the best treatment for the burn; compromise was often found to be necessary because of the combination of injuries.

From experience gained in treating associated burns and fractures from flying accidents among Royal Air Force personnel in World War II, Bodenham stated in 1943 that the burn should be treated by pressure dressings combined with elevation of the part. Because reduction of the fracture may produce shock, Bodenham suggested that one manipulation, with approximate reduction, is sufficient until the patient's general condition improves. He stated that pins must not be put through burned areas because of the risk of bone infection and, therefore, immobilization by plaster is necessary except for fractures of the femur, where traction is required.

Warthen pointed out in 1944 that many of these combined injuries result in death before medical aid can be given. Based on experiences at U. S. Army Air Fields during World War II, he expressed the opinion that plaster encasement had proved a satisfactory method of treating these combined injuries except for injuries of the thigh. Skeletal traction was advocated for the treatment of fractures of the femur complicated by burns; 3 such patients were successfully treated by skeletal traction. In one of these patients the wire was inserted through burned skin but infection did not develop.

Urist and Quigley have reported their experience during World War II with 15 armored corps battle casualties having severe burns of one or two limbs associated with open fractures. In all instances the patients were transported by air ambulance in plaster casts, and immediately suspended in skeletal traction on arrival in the United Kingdom. The reaction of the burned skin and underlying bone to the Kirschner wire used for traction



a b Fig. 4.

Fig. 3.

Fig. 3. Two samples of similar closed fractures of radius and ulna of both forelegs produced by the fracturing apparatus. a, Dog 618, roentgenograms of right and left forelegs taken shortly after injury. b, Roentgenograms taken several weeks after injury was produced. The right leg, shown on the left, has been immobilized with plaster and wire ladder splints. The left leg, shown on the right, has been immobilized by insertion of an intramedullary nail in the radius.

Fig. 4. Closed fractures of radius and ulna. Roentgenogram taken immediately after open reduction and intramedullary nailing of the radius. Dog 625.

was not determined. Wires were not inserted through burned skin; if the site of election for insertion were burned, a compromise was made in the treatment of the fracture by inserting the wire distal to the point of election, through normal skin. The authors emphasized that a wire put through burned skin would almost surely produce an infected tract, but thought that the infection would probably not be of long term significance.

Not all writers have advocated plaster casts for associated burns and fractures. Watson-Jones stated: "If an unpadded plaster cast, or even a padded cast, is applied on the first day of injury, gangrene is almost inevitable. Every such case dealt with in the Royal Air Force orthopaedic service during the recent war was complicated by gangrene and amputation of the limb when plaster was used during the first 24 hours. Even apart from the immediate danger of ischaemia due to pressure of the plaster, there is a later danger of lymphatic spread of infection from the burnt skin and subcutaneous tissues to the undrained hematoma of the fracture. The problem of treatment may thus be increased very greatly by infection of the fracture and the bone. No matter how great the difficulties of immobilizing the limb, a complete plaster cast should not be used. The first objectives are the treatment of the burn, the control of infection, and the replacement of skin, and in achieving these ends it matters little that deformity may arise; it is easy to correct deformity by later reconstructive operations, but it is not possible to replace a limb that has been amputated." We should like to point out, however, that unrestricted motion of the bone ends may be a potent force in the production of spreading soft tissue and bone infection and that some safe method should be sought for immobilizing fractures associated with burns.

EXPERIMENTAL METHODS USED IN THIS STUDY

General. We attempted to simulate conditions of atomic warfare. Burns and fractures were produced simultaneously, and 20 hours later débridement was performed and the injuries treated. We selected this time lag be-

a b

Fig. 5. Ulna fractured bilaterally at junction of middle and distal thirds with a Gigli saw. Roentgenograms taken immediately after treatment. a, Right side, no immobilization has been applied. b, Left side, a stainless steel Kirschner wire has been inserted in the medullary canal for immobilization of the fracture.

cause it seems unlikely that analogous injuries in the human can be treated immediately after occurrence, hence any experimental method should be tested after a period of delay.

Mongrel dogs weighing from 6 to 15 kilograms were observed for a period of 3 weeks before being subjected to the experimental procedure. During this period each dog was given two 20 cubic centimeter injections of homologous anticanine distemper serum and a 5 day course of oral sulfamerazine, 1.5 grams daily. Only dogs that had been given this preparation and that appeared to be in good general condition at the end of 3 weeks were subjected to the experimental procedure. After the experimental procedure all dogs were given 100,000 units of penicillin intramuscularly daily for 5 consecutive days.

Method of producing burns. Following anesthetization with intravenous nembutal, both forelegs between the paws and elbows were burned by immersion in water at 90 degrees C. for equal periods of time, varying from 7 to 10 seconds. The paws were protected from burning by wrapping with thick rubber gloves. The area to be burned was shaved before burning. The burning apparatus which we used (Fig. 1) was developed by McCarthy for producing a standard burn in the rat.

Method of producing and treating fractures. Closed fracture series.—An apparatus was developed for producing similar closed fractures of the radius and ulna of the dog. The fracturing apparatus shown in Figure 2 has a tripod base and a supporting upright column in its center. From the upright column projects an arm which can be adjusted in height. From this arm is hung a smooth rounded metal rod (5 feet long and ½ inch in diameter) and welded to the arm so that it hangs perpendicular to the floor. The fracturing force is produced by allowing a weight (5.3 kgm.) to fall a given distance on this rod. The center of the weight is bored out so that it slides smoothly over the rod. In order to have the fracturing force applied over a small area rather than over the large surface of the weight, a hole, approximately 4 inches deep, was drilled in the center of the lower end of the rod. Into this hole fits the shaft of a narrow T shaped piece of metal with the crosspiece projecting 1½ inches from the bar on each side. The dog's foreleg was suspended between two wooden blocks with the ulnar side up. The T shaped crosspiece was placed at the site to be fractured and the weight allowed to fall on it. We found a suitable distance for dropping the weight to be about 60 centimeters. The weight was allowed to strike the lateral side of the foreleg a little distal to its center. Figure 3a, b shows 2 examples of similar fractures of both forelegs produced by this apparatus.

No immediate immobilization was applied to any of these fractures. Twenty hours after injury the dogs were reanesthetized. On the right side the fractures were reduced by closed manipulation and immobilized with wire splints supplementing plaster of paris splints. Dry sterile gauze dressings were used to cover the burns. On the opposite (left) side an open reduction of the radius was performed through the burn area under sterile conditions. The fracture was exposed and a stainless steel Steinmann pin was driven through the distal fragment's medullary canal with the tip emerging at the dorsum of the flexed wrist. When the end of the pin had reached

TABLE I.—HEALING OF BURN—CLOSED FRACTURE SERIES (15 DOGS)

Months required for complete healing

Dog No.	Left leg—intramedullary nail Burn left open	Right leg—plaster fixation Burn covered with plaster
619	1½	2
625	1½	Not healed at sacrifice (3 mos.)
784	1½	Not healed at sacrifice (3 mos.)
845	1½	1½
785	2	2
957	1½	2
954	1	1
955	Died distemper 10 days, healing well	Died distemper 10 days, infected
847	Healing satisfactorily at death, 1 month	Died from sepsis 1 month. Spreading infection, R. leg
850	Healing satisfactorily at death, ½ month	Died from sepsis ½ month. Spreading infection, R. leg
849	Healing satisfactorily at death, ½ month	Died from sepsis ½ month. Spreading infection, R. leg
786	Healing satisfactorily at death, ½ month	Died from sepsis ½ month. Spreading infection, R. leg
848	Healing satisfactorily at death, ¾ month	Died from sepsis ¾ month. Spreading infection, R. leg
952	Healing satisfactorily at death, (80% epithelialized) 1 month	Died from sepsis 1 month. Spreading soft tissue infection, R. leg
618	Healing satisfactorily at death, ½ month	Died from sepsis ½ month. Spreading soft tissue infection, R. leg

TABLE II.—HEALING OF BURN—OPEN FRACTURE SERIES (15 DOGS)*

Months required for complete healing

Seven dogs treated with plaster on right leg			Seven dogs treated without plaster		
Dog No.	Left (intramedullary nail)	Right (plaster)	Dog No.	Left (intramedullary nail)	Right (no plaster)
	Burn left open	Burn covered with plaster		Burn left open	Burn left open
181	1½	5	132	3½	3½
186	1	4	184	1	1
250	1½	3½ (unhealed at death)	239	1	1
370	1½	2	379	2½	2½
376	1	2½	438	2	2
378	1½	3	502	2	2
503	2	5	252	2	2
Average	1½	3½		2	2

*Dog 375 died 3 weeks after operation from distemper and before significant healing of burn had occurred.

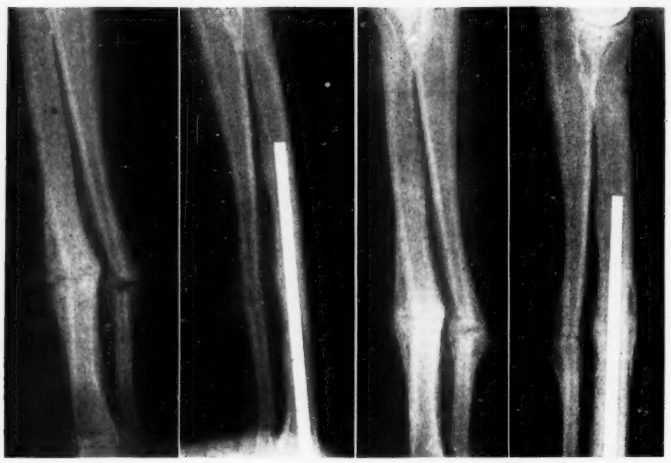
he fracture site, the fracture was reduced and he pin driven back into the medullary canal of the proximal fragment until good stability was obtained. After withdrawing the pin a few millimeters, the excess of pin beyond the skin was cut off and the pin driven back into bone with a nail punch so that full motion of the joint was possible (Fig. 4). The fascia was then closed and the skin left open. No dressing was applied to the burns. Fixation of the radius by this method gives such good stability of both bones that no further immobilization is needed. Splints and gauze dressings were changed on the unnailed side at 1 to 2 week intervals.

Open fracture series.—Open fractures were produced in both ulnae with a Gigli saw without fracturing the radius. Such fractures, if produced at the junction of the middle and distal thirds, are relatively stable and will unite without additional immobilization because of the intact radius and interosseous membrane. The open fracture preparation allowed us to test the complication of burning in a relatively stable fracture in contrast to the closed fractures which were unstable unless rigidly fixed. Union is delayed because of bone loss from the Gigli saw and the resulting distraction that is maintained by the intact radius.

The technique of fracturing was as follows: Immediately following burning, both ulnae were exposed by a 2 inch incision through the burn and were fractured transversely with a Gigli saw approximately at the junction of the middle and distal thirds (Fig. 5). An attempt was made not to denude the bone of periosteum. Aseptic technique was *not* employed during the operation, and the skin was closed with silk thereby increasing the opportunity for infection. Twenty hours after the trauma and after repeating the anesthesia, the wounds on both sides were opened and débrided under sterile conditions. On the left side a stainless steel Kirschner wire was inserted at the fracture site through the proximal fragment and out the olecranon. When its end had reached the fracture site, the fracture was reduced and the wire then inserted into the distal fragment by drilling from the olecranon. The subcutaneous tissues

Fig. 6.

Fig. 7.



a b

Fig. 8.

Fig. 6. Dog 485. Photograph taken 2 weeks after burning and fracturing (bilateral closed fracture of both radii and ulnae). Right leg immobilized by plaster and wire splints. Radius of left leg fixed with intramedullary nail. The burn covered with plaster (right side) is largely unhealed while the burn left open is almost completely epithelized.

Fig. 7. Dog 250. Photograph taken 8 weeks after burning and fracturing (open fracture of both ulnae). Complete healing of burn on left side where the fracture had been nailed and the burn left open. Large area of granulation on right side where the burn had been covered with plaster.

Fig. 8. Roentgenograms of both sides at 8 and 10 weeks after bilateral fractures. Good healing of both sides is demonstrated. a, At 8 weeks. b, At 10 weeks.

were closed and the skin left open. On the opposite side (right side) no wire was inserted but the soft tissue wound was similarly débrided and the subcutaneous tissue closed. In 8 dogs plaster splints were applied to the unnailed side after covering the burn with sterile dry gauze and reapplied at intervals of about 2 weeks. In the remaining 7 dogs no immobilization was used on the unpinned side, and the burns were left exposed. No dressings were applied to any of the nailed forelegs, and no external means of immobilization were used.

RESULTS

Results were determined by physical examination of the dogs at frequent intervals, microscopic examination of sections from the burned skin, roentgenograms of the legs at intervals of about 2 weeks, culture of exudates from the burned surface, and microscopic examination of sections of bone at and adjacent to the fracture site after death of the dogs.

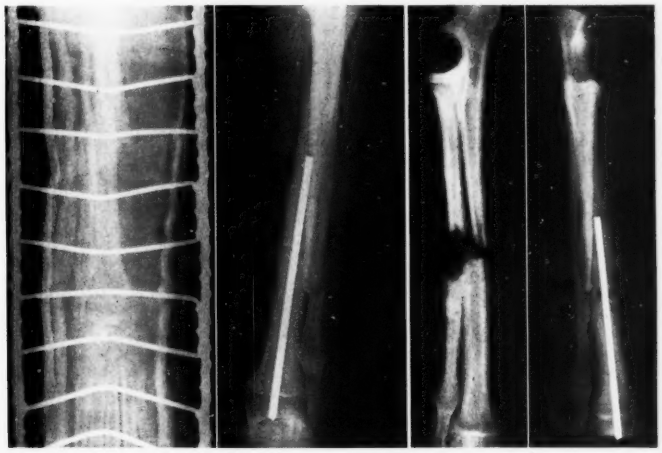


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Fig. 9.

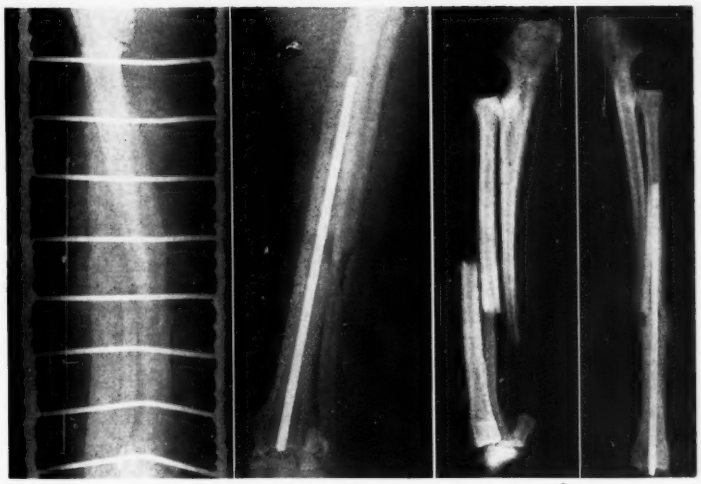

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Fig. 10.

Fig. 9. Evidence of bone infection in poorly immobilized extremity. a, Roentgenograms taken immediately after burning and fracturing. Left side treated with open reduction and intramedullary nailing, right side by immobilization with plaster and wire ladder splint. The right side is not as well reduced as the left. b, Taken 2½ weeks later immediately after death caused by a spreading soft tissue infection of the leg covered by plaster "disruption" of the fracture. Note evidence of bone infection on the side covered by plaster, which was confirmed microscopically.

Fig. 10. Dog 786. a, Roentgenograms taken day after operation. Left foreleg fractures fixed by open reduction and nailing with intramedullary nail. Right foreleg fractures have been reduced by closed reduction and are being held with plaster and wire ladder splint. b, Roentgenograms taken 2 weeks later, immediately after death due to spreading soft tissue infection on the side immobilized with plaster. Complete disruption of the fractures occurred on the side covered by plaster due to spreading soft tissue infection and muscle necrosis.

The burn wound. As determined by microscopic examination of the burned skin at 20 hours after burning, the average burn was of deep second degree with most of the hair

a b

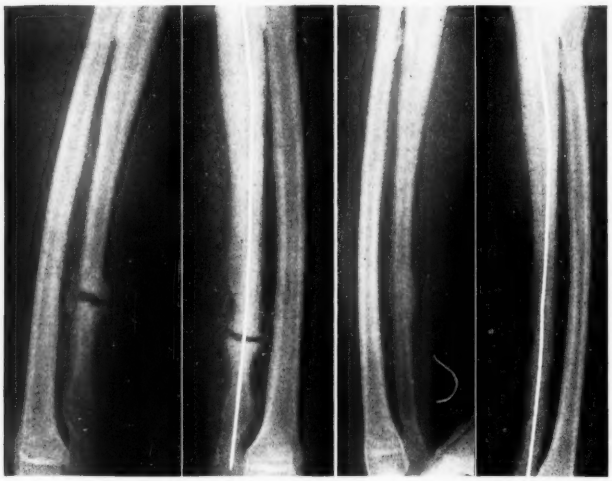

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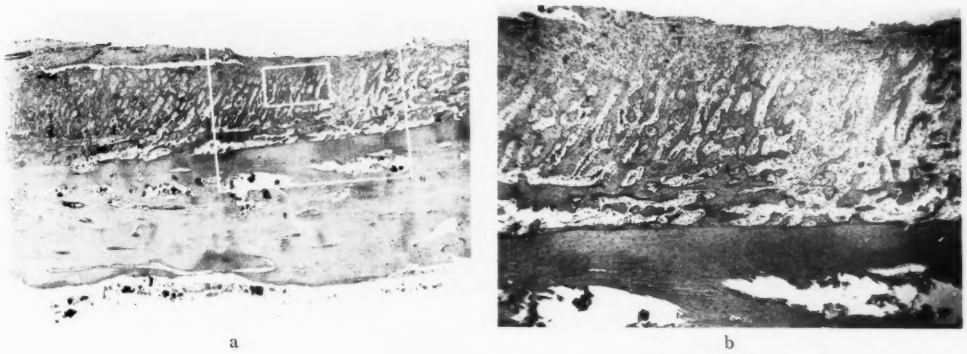
Fig. 11. Roentgenograms taken at intervals following burning and fracture of both ulnae at junction of middle and distal thirds with a Gigli saw. Delayed union on both sides, thought to be due to bone loss and distraction. a, X-ray films of right and left leg taken shortly after injury. Intramedullary nail introduced into medullary cavity of left leg but no immobilization of right leg. b, Roentgenograms taken 2 weeks after fracture. Right leg, slight absorption of bone of both fragments at fracture site. Left leg, considerable periosteal bone formation along almost the whole of the proximal fragment. c, Roentgenograms taken 5 weeks after fracture. Right leg, new bone formation at ends with incomplete bridging of fracture site. Left leg, some absorption of periosteal new bone has occurred. d, Roentgenograms taken 15 weeks after fracture. Both legs, roentgen evidence of complete healing of fracture on both sides.

follicles and sebaceous glands destroyed but with some appendages viable in the skin depths. Little variation was observed in the depth of burn between different dogs.

One of the most striking results of this study was the deleterious effect of covering the burn with gauze and plaster. This effect was noted in both the open and the closed



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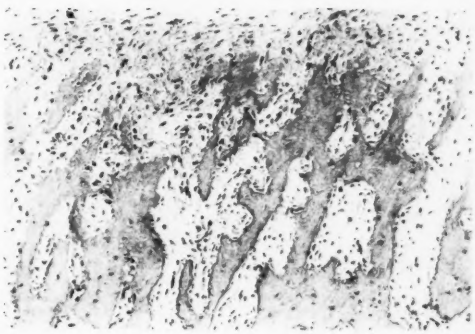

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Fig. 12. Three photomicrographs of left ulna of dog 75 which died of distemper 3 weeks after injury. The sections were taken through periosteal callus similar to that seen in Figure 11. Note that the callus is made up of transversely trabeculated bone. Three magnifications are shown, the two higher magnifications taken from the blocked out areas shown in photomicrograph, a. a, Lowest magnification showing cortical bone at the bottom, covered with periosteal callus made up of transversely trabeculated bone. b and c, Taken from the blocked out areas shown in a. b, Photomicrograph of larger block in a, showing cortical bone below and transversely trabeculated bone above. The transversely trabeculated bone is the periosteal callus seen in the roentgenogram. c, Photomicrograph of smaller block in a. Higher magnification of transversely trabeculated bone.

fracture series. In almost every instance in which plaster was applied to the forelegs, healing of the burn was delayed as compared to the opposite, uncovered side. In some instances one of a pair of identical burns was converted into a full thickness burn when covered with gauze and plaster while the opposite side, left exposed, remained superficial. Plaster was not applied to 7 unnailed forelegs in the open fracture series. The burns in these 7 uncovered legs remained of the same depth and healed in the same time as those of the opposite, nailed leg. It must be noted that only the ulna was broken in the open series and the intact radius and interosseous membrane gave good stability to the foreleg without added fixation.

The next two illustrations (Figs. 6 and 7) illustrate the remarkable retardation of healing and the conversion of an original second degree burn into a third degree burn by covering with gauze and plaster.

All of the burns became contaminated with several varieties of bacteria, the most common being hemolytic Staphylococcus albus, hemolytic Staphylococcus aureus, Bacillus subtilis, diphtheroids and Escherichia coli.

Closed fracture series (15 dogs). Both forelegs of 15 dogs were burned and both radii and ulnae were fractured by the fracturing apparatus, as described previously. On one side the fractures were reduced by closed manipulation and immobilized with wire ladder splints superimposed on plaster of paris splints after the burns were covered with sterile gauze dressings. On the opposite side the burns were left exposed, and the fracture of the radius was reduced by an open operation and immobilized with a stainless steel intramedullary nail.

Figure 8a, b is a series of roentgenograms of dog 954 taken at 8 weeks and 10 weeks after bilateral closed fracture of both bones of the foreleg at the time of burning. The bones of

Fig. 13. Roentgenogram of dog 378 following death from distemper 3 months after injury. Union has not occurred on either side.

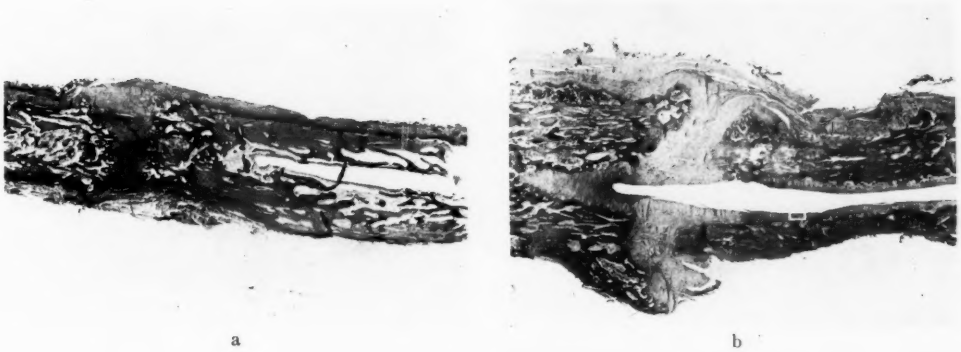
the left leg were immobilized by the intramedullary nail in the radius. It is noted that the ulna is held in good position by the well stabilized radius and goes on to heal in good position. The right foreleg fractures were reduced by closed manipulation and immobilized by wire ladder and plaster splints. Healing also progressed satisfactorily, and good union took place with slight malalignment. No bone infection was noted on either side.

The following observation we considered of probably the greatest importance in this study. Although 7 of the "burn-fracture" forelegs treated by plaster immobilization healed satisfactorily, 7 of the 15 dogs treated by this method died within 4 weeks from severe infection of the leg treated with plaster. These legs showed extensive muscle necrosis and exposure of the fracture site (delayed compounding from within) because of a combination of spreading soft tissue infection and lack of rigid fixation of the fracture. Once the spreading soft tissue infection became established, such severe muscle damage occurred that no stability of the bone fragments could be maintained and disruption of the bones occurred not withstanding the presence of the plaster and wire splints. This was in striking contrast to the better stabilized bones on the pinned side where the burns were left uncovered. No spreading soft tissue infection occurred here, and no significant bone infection on this side was found at autopsy. Figures 9 and 10 show 2 examples of complete separation of the fracture on the sides covered with plaster caused, we believe, by a combination of spreading soft tissue infection and unstable bone fragments. We postulate that a vicious circle starts once soft tissue infection begins to spread. The poorly stabilized bone fragments increase the soft tissue damage which in turn allows greater motion at the fracture site and eventually leads to complete disruption of the fracture. Severe osteomyelitis was found on microscopic examination of the bones on the side immobilized with plaster in several instances while the side immobilized with the nail was relatively clean.

If the vicious circle of spreading soft tissue infection and bone instability did not begin, then the fractures healed satisfactorily on the side covered with plaster. This occurred in 7 instances.

Open fracture series (15 dogs). The results in the open fracture series were in striking contrast to those in the closed series due, we believe, to the fact that only the ulna was fractured in the open series and the fragments were relatively stable without any added fixation. None of the dogs in this series died from the severe soft tissue and bone infection which occurred in 50 per cent of the closed series when an unstable fracture contaminated with a burn was covered with plaster.

Two of the 15 dogs died of distemper at 3 and 12 weeks respectively after trauma, and the remaining 13 dogs were sacrificed at varying lengths of time after operation. In every instance in which plaster was applied healing of the burn wound was delayed and the average time required for healing approximately doubled. Infection at the fracture site was not obvious on the roentgenograms or by gross inspection in any instance. The fractures healed slowly in all dogs, whether nailed or unnailed, with plaster or without (see Table IV). The fact that the intact radius maintains separation of the ulnar fragments caused by bone loss from the Gigli saw almost certainly accounts for the delayed healing. Fig-



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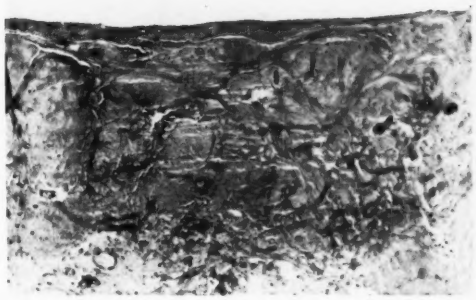

c

Fig. 14. Photomicrographs of both ulnae of dog 378 whose roentgenograms were shown in Figure 13. Fibrous union of both ulnae is noted. Leucocytic infiltration is present on the unnailed side, a. No evidence of infection is seen on nailed side, b. c, A section from the endosteal side of the cortex adjacent to the nail (small block in b) and illustrates the lack of reaction to the presence of the nail. a, Photomicrograph of right ulna. Note fibrous union on the left side of photomicrograph. b, Photomicrograph of left ulna. Note fibrous union and minimal leucocytic reaction. The small blocked out area is seen in c. c, Photomicrograph covering blocked out area in b. Note lack of reaction to the presence of the nail. There is a fibrous tissue lining for the pin, but no evidence of infection.

ure 11 presents a series of roentgenograms showing delayed union on both sides. Of special interest is the periosteal reaction away from the pin site which is well seen in Figure 11b. Microscopic examination of such callus shows transversely trabeculated bone, as illustrated in 3 magnifications in Figure 12. We have called attention to this reaction in a previous publication (3) and postulated that it is due to pressure of a foreign body on the endosteum. Infection is not a factor in its production as far as could be determined by these experiments.

In general, the burns have not retarded the healing of the fractured ulnae as judged by a comparison of the healing times for the fractures in these experiments (complicated by experimental burns) with previously reported fractures of the ulna (3, 8) not complicated by burns.

Infection of the bone was not observed microscopically to have been increased by insertion of the intramedullary wire. Figure 13 shows roentgenograms of the ulnae of dog 378 that died of distemper 3½ months after injury. Union had not occurred on either side. Figure 14a, b, c presents photomicrographs of the ulnae of dog 378. Bony union had not occurred on either side, and the bone ends were seen microscopically to be joined by fibrous tissue. Little reaction to the insertion of the nail is observed on microscopic examination (Fig. 14c). A fibrous tissue lining is noted along the nail site.

Healing of the fractures occurred more slowly on the nailed side in the majority of the dogs but infection did not seem to be responsible for this delay in union. We had not seen this delay on the nailed side in our previous work on unburned limbs (3, 8) but do not believe it is directly related to the burning since burning did not increase the time of healing on the unnailed side as compared to identical fractures in unburned dogs in

TABLE III.—HEALING OF RADIUS—CLOSED FRACTURE SERIES

Months required for bony union

Dog No.	Left—intramedullary nail	Right—plaster fixation
619	1½	1½
625	1½	1½
784	3	3
847	1	Ununited at death, 1 month
845	1¾	1¾
785	2½	1½
957	2	3
954	1	1½
850	Signs of union—death 2½ wks.	No signs of union—bones exposed
849	Signs of union—death 2 wks.	No signs of union—bones exposed
786	Signs of union—death 2 wks.	No signs of union—bones exposed
952	Beginning union—death 1 mon.	Beginning union
618	No sign of union—death 10 days	No sign of union—bone exposed
848	Beginning union—death 3 wks.	Beginning union—death 3 wks.
955	No sign of union—death 10 days	No sign of union

TABLE IV.—HEALING OF ULNA—OPEN FRACTURE SERIES (15 DOGS)*

Months required for bony union

Technical difficulties in nailing 6 dogs			No technical difficulties in nailing 8 dogs		
Dog No.	Left (nailed)	Rt. (unnailed)	Dog No.	Left (nailed)	Rt. (unnailed)
182	4½	2½	181	3¾	3
184	Ununited at death, 8 months	6½	186	6	6
239	Ununited at death, 3½ months	3½	370	Ununited at death, 8 months	3
250	Ununited at death, 3½ months	2½	376	3	2½
252	Ununited at death, 3 months	3	379	2	2
503	Ununited at death, 5 months	5	378	Both ulnae ununited at death from distemper, 3 months	
Average		4	438	2¾	2¾
			502	2	2

*Dog 375 died 3 weeks after operation from distemper.

the previous studies. We believe it was caused by faulty technique in nailing. In 6 instances we believe the delay in union on the nailed side was due to technical difficulties arising from the presence of a medullary canal too small to accommodate our smallest nail. Early in the experiment we selected smaller dogs than we had used previously. In 5 of the 6, union was not solid at the time of sacrifice of the dog (Table IV). As noted in Table IV, when larger dogs were used and no technical difficulties were encountered, the ulnae healed in approximately the same time on both the nailed and unnailed sides. Of interest is the fact that in 2 instances in which a very small medullary canal was observed the relatively large nail seemed to produce an early avascularity of the bone fragments on both sides of the fracture. This avascularity was manifested by an increase of density of the bone fragments on each side of the fracture, and we anticipated sequestration of the bone; yet in each instance the avascular bone was absorbed and did not sequestrate. In spite of the wide gap that resulted at the fracture site, one of the ulnae went on to bony union. Figure 15 shows a series of roentgenograms of the nailed ulna of one of these dogs.

A critique of experimental results. Under the conditions of these experiments in dogs, open reduction and insertion of an intramedullary nail through burned skin did not increase soft tissue or bone infection when compared to a control side treated by immobilization with plaster of paris. This was true in both open and closed fractures. The fact that fixation with an intramedullary nail allowed the burn wound to be left open resulted in better healing of this wound on the nailed side in practically every instance. In 7 dogs of the closed fracture series in which both radii and ulnae were fractured spreading soft tissue infection and imperfect fracture fixation on the unnailed side led to muscle necrosis, delayed compounding from within, and death of the animal. The opposite, nailed side did not become infected, and the fracture remained stable.

Do these facts allow us to conclude that intramedullary nailing is an acceptable method for the treatment of burn fracture trauma in the human? The following criticisms could

a b c d

Fig. 15. Early roentgen evidence suggests sequestration but absorption takes place and later films show new bone formation. a, Roentgenogram taken at 2 weeks after fracture. Marked periosteal new bone formation and some resorption of bone seen in both fragments. b, Roentgenogram taken at 6 weeks after fracture. Further resorption of bone leaves a "bone island" which suggests sequestration. c, Roentgenogram taken 18 weeks after fracture. Still further resorption of bone including "bone island" and some evidence of new bone formation at ends of both fragments. d, Roentgenogram taken 20 weeks after fracture. X-ray film made of disarticulated limb shows definite evidence of new bone formation at ends of fragments.

be made with accuracy in applying the results of these experiments in dogs to the problem in man.

1. A comparison of open versus closed treatment of burns in dogs differs greatly from the human. It is impossible to immobilize completely the leg of the dog with plaster, and it was felt that in some instances rubbing of the plaster against the burn wound further traumatized it. In addition the dogs kept the burn on the open side free of exudate by licking and could not so "treat" the burn covered with plaster. In the human, where better immobilization could be effected with plaster, such a striking difference might not occur between the open and closed sides.

2. For many fractures in the human there are probably better methods of treating a fracture complicated with a contiguous burn than the closed plaster technique—for example, balanced skeletal traction—whereas our experiments compared intramedullary nailing with only the closed plaster technique.

3. Bones of the dog are said to be more resistant to infection than those of the human, and the lack of infection in the nailed bones in these experiments might not be observed in analogous situations in man. (Yet, one of us, M.W.A., as Professor of Surgery in the Veterinary School of Medicine, has seen many dogs with osteomyelitis after open fractures).

Notwithstanding the fact that these experiments have many deficiencies when any application to the human is attempted, we believe they do show that rigid immobilization of contaminated bone is of great importance in the prevention of bone and soft tissue infection. If rigid immobilization necessitates open reduction and internal fixation, the risk of infection from operation, even through burned skin, may be less than the risk of using closed methods which do not fix the fracture securely and which may preclude the best methods for treatment of the burn.

SUMMARY AND CONCLUSIONS

1. Experiments were performed in dogs comparing intramedullary nailing with external plaster fixation in treating fractures of the radius and ulna complicated by overlying burns of the skin.

2. The open treatment of the burned skin was found to be preferable to covering the skin with gauze and plaster under the conditions of these experiments.

3. The introduction of an intramedullary nail through burned skin did not increase bone infection.

4. Spreading soft tissue and bone infection did not occur when the bones were rigidly fixed by an intramedullary nail and the burn left open, but did occur in one half of the legs when unstable fractures complicated by burns were fixed with plaster.

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INTUSSUSCEPTION URETERECTOMY: A METHOD OF REMOVAL OF THE URETERAL STUMP AT TIME OF NEPHRECTOMY WITHOUT AN ADDITIONAL INCISION

DONALD F. McDONALD, M.D., Seattle, Washington

THE common practice of leaving a 10 to 15 centimeter length of lower ureter at the time of nephrectomy often makes necessary later excision of the ureteral stump. This is especially true if the ureter is diseased. In 880 cases of nephrectomy for stones, Bumpus and Scholl reported the need for ureterectomy in 51 patients, an incidence of 5.8 per cent. Senger, Bell, Warres, and Tirman routinely studied 22 ureteral stumps after nephrectomy and found 1 case of tuberculous empyema, 2 cases of nonspecific empyema, and 2 cases of calculi, a 23 per cent incidence of unfavorable results. They found reflux of contrast material up the ureteral stump upon cystography in only 1 instance. Lack of reflux is additional evidence to support the views of Livermore who believes calculi do not form in the ureteral stump but are left there at the time of nephrectomy.

The disease processes which eventually necessitate the removal of the ureteral stump are largely those related to the condition which required nephrectomy. This is an indication that total ureterectomy should be done more often at the time of nephrectomy. Reiser collected 37 cases of pyoureter 17 of which were related to ureteral calculi possibly left in at time of nephrectomy. London reported acute empyema of a ureteral stump due to calculus 20 years after nephrectomy. Stepita and Newman reported 15 cases of empyema and listed the diseases of the ureteral stump as stricture, dilatation, calculus, tuberculosis, and neoplasm. Kidd, Kimbrough, and Bailey, Fort, and Harlin report recurrent papillary carcinoma of the ureteral stump in 80 to 100 per cent of cases of papillary carcinoma of the renal pelvis treated by simple nephrectomy. Squamous carcinoma developing in the chronically infected ureteral stump 14 years after nephrectomy has been reported by Loef and Casella. McMahon has reported a similar case related to the presence of a calculus of the ureteral stump 20 years after nephrectomy. Rieser, and Azagra, Gorro, and Serra find that tuberculosis of the residual ureter usually results in obliteration of the lumen and in healing in about 2 years, but the condition may lead to empyema. Hunt reported 574 cases of nephrectomy for renal tuberculosis in none of which was ureterectomy required. Experimentally, Latchem found that obstruction was the most important cause of persistent infection in the ureteral stump. Age does not alter the indications for ureterectomy. Ljunggren has reported 2 cases of nephrectomy in children, 1 year of age, whose ureteral stumps remained chronically infected. One had reflux of urine, developed a calculus, and had a ureterectomy 2 years later. The other had a chronic urinary infection which resulted in uremia of the remaining kidney and death 7 years later.

The diagnosis of disease of the ureteral stump is not always obvious. The presence of lower quadrant unilateral pain or colic, especially when there is associated recurrent cystitis with pyuria, frequency, and dysuria, should cast suspicion on the ureteral stump. Catheterization of the ureteral stump permits aspiration of its contents for microscopic and bacteriologic study. Visualization by retrograde ureterography usually makes possible the diagnosis. When catheterization is not possible as obtains in cases of stricture and empyema, purulent material can sometimes

From the Division of Genito-Urinary Surgery, the University of Washington School of Medicine, Seattle, Washington.

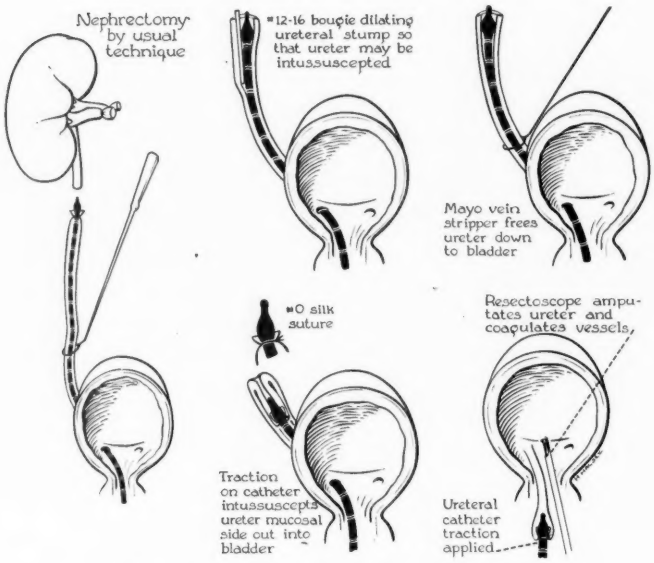
Nephrectomy by usual technique
#12-16 bougie dilating ureteral stump so that ureter may be intussuscepted
Mayo vein stripper frees ureter down to bladder
#0 silk suture
Resectoscope amputates ureter and coagulates vessels
Traction on catheter intussuscepts ureter mucosal side out into bladder
Ureteral catheter traction applied

Fig. 1. Technique for intussusception ureterectomy.

be seen extruding from the narrowed orifice, as described by Fowler.

The classical aseptic method of Beer for extirpation of the entire ureter at the time of nephrectomy has been the procedure most frequently used. The chief disadvantage of this technique is that it requires repositioning and redraping of the patient and a second incision. It is, however, preferred to the extensive incision from the costovertebral angle to the inguinal ring employed by some. A modification of Beer's technique, making certain of excision of the ureteral orifice, is proposed by Patton. McDonald, Upchurch, and Sturdevant have suggested transurethral amputation of the ureterovesical junction with the resectoscope prior to ureteronephrectomy. This procedure has not been generally accepted because it permits contamination of the retroperitoneum with ureteral contents and produces a muscular defect in the bladder wall.

The number of secondary ureterectomies reported in the literature, although not numerically great, shows that the indications for ureterectomy are not generally appreciated. It may also indicate that many times, although the surgeon realizes that total ureterectomy is desirable, he is reluctant to subject the patient to an additional or more extensive incision. The ureter probably does not have to be totally removed routinely. However, in cases in which infection, dilatation, or stricture is present in the lower ureter a total ureterectomy should certainly be performed. When nephrectomy for papillary carcinoma of the renal pelvis is performed the lower ureter must be excised to obviate the need for later excision since recurrence of tumor in the stump is the rule. The best course to follow with respect to the lower ureter is that advocated by Rieser—if in doubt remove it. A simple procedure for ureterectomy would accomplish the desired result without risk. To that end the following procedure is suggested.

METHOD

A ureteral bulb-tip catheter is passed, preferably preoperatively (Fig. 1). In 1 clinical case this was not done preoperatively and a catheter was passed backward, down the ureter, at time of nephrectomy. Later, at time of electroresection it was withdrawn cystoscopically. After nephrectomy is performed in the

Fig. 2.

Fig. 2. Dog 1, stump of ureter and vesical calculus when ureter was intussuscepted into bladder and not resected.
Fig. 3. Calculus pyonephrosis showing additional length of ureter removed by intussusception ureterectomy.

Fig. 3.

usual manner, the intubated ureteral stump is dilated to admit a No. 16 French catheter, if possible, so that it will invert and pass through its intramural portion into the urinary bladder. The cut end of the ureter is then sutured to the ureteral catheter, the suture passing just below the bulb of the ureteral catheter. A blunt Mayo vein stripper is then passed down the outside of the ureter to the ureterovesical junction to mobilize the ureter from its retroperitoneal attachments. The portion of the ureteral catheter protruding from the urinary meatus can then be grasped, and by means of traction the ureter may be gently intussuscepted into the urinary bladder. After closure of the nephrectomy incision the patient is placed in position for cystoscopy. With traction applied to the ureter it is a simple matter to amputate the redundant ureter with one stroke of the resectoscope loop. No intramural ureter remains and no bladder wall need be resected. Any bleeding that takes place may be controlled by means of the coagulating current.

RESULTS

Dogs. In dog 1 the ureteral stump was intussuscepted by traction on the ureteral catheter. The stump was allowed to remain in the bladder. Four weeks later (Fig. 2), there was a well vascularized stump remaining and a vesical calculus with a portion of sloughed ureter as its nidus.

The intussuscepted ureteral stump in dog 2 was amputated. At 4 weeks there was no abnormality except absence of a ureteral orifice.

Humans. Of 3 human cases so treated, 2 were completely successful without complication 1 year or more after surgery. In 1 case the ureter had not been dilated adequately. The ureteral catheter pulled free as the ureter was about to come into the bladder. In this patient, however, no complications ensued. Figure 3 shows the additional length of ureter removed by the present technique.

SUMMARY

A new method of removal of the ureteral stump without an additional incision is sug-

gested for routine removal of the ureteral stump usually left behind after nephrectomy.

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BILATERAL TOTAL ADRENALECTOMY IN PATIENTS WITH METASTATIC CARCINOMA

HARVEY KRIEGER, M.D., WILLIAM E. ABBOTT, M.D., STANLEY LEVEY, Ph.D., and LOUIS BABB, M.D., Cleveland, Ohio

THE rationale for the use of bilateral adrenalectomy as a therapeutic measure for metastatic carcinoma is based upon both clinical and experimental observations. It is a well known fact that the growth of both breast and prostatic carcinoma is influenced by alteration of the sex hormone pattern, and that hormones have been used with some success in the treatment of metastatic carcinoma of the breast and prostate. The relapse which occurs in patients who have been castrated or have received hormone therapy is thought to be the result of androgen production by the adrenal cortex. Dobriner and his associates have demonstrated that patients with cancer excrete abnormal amounts of steroids in the urine.

The present report is based on data obtained from a group of 5 patients with metastatic carcinoma. Three of the patients had carcinoma of the breast as the primary lesion, 1 patient had carcinoma of the prostate with skeletal metastases, and the fifth patient had widespread melanosarcoma. First the preoperative and postoperative management of these patients will be discussed, and the data on the clinical and metabolic alteration following bilateral total adrenalectomy will be presented. In accordance with the findings of Huggins and Dao and West and his associates, the patients with carcinoma of the breast demonstrated for varying periods of time an increased feeling of well being, increased appetite, and relief from pain.

The patients included in this report were admitted to the metabolic division of University Hospitals of Cleveland and were studied both preoperatively and postoperatively. Other more accepted forms of therapy had been or were tried prior to performing total adrenalectomy.

All food and fluids consumed by the patients were carefully prepared and measured by the dietitian in charge of the metabolic division. These substances, as well as all parenteral solutions used, were analyzed by accepted methods for the calcium, nitrogen, chloride, sodium, and potassium content. The collection of urine was carried out in 24 hour periods, and all stool, emesis, and other excreta pooled in 4 day periods and suitable aliquots were analyzed.

SURGICAL TECHNIQUE

A brief description of the operative technique employed in these cases is presented. Either continuous spinal or endotracheal gas-oxygen-ether anesthesia was used. Endotracheal anesthesia may be preferable because of the possibility of accidently opening the pleura. The patient was placed in the prone position and both glands were removed simultaneously, 2 operating teams being used. The twelfth rib was resected through a posterior oblique incision. After incising Gerota's fascia, the kidney, surrounding fat, and adherent adrenal gland were mobilized en masse and retracted down into the wound. In order to insure complete removal, since the adrenal gland is very friable, it was not grasped by an instrument but all attachments were freed by sharp dissection, the adrenal veins clamped, ligated, and divided, and as the last step the gland was separated from the upper pole of the kidney. The right adrenal vein is shorter than the left and it is sometimes difficult to ligate. Blood samples from the adrenal have been taken by inserting a sterile polyvinyl catheter into the left adrenal vein. The concentration of the various steriods found in the blood of the adrenal vein will be discussed in another paper. It usually takes approxi-

From the Department of Surgery, School of Medicine, Western Reserve University and University Hospitals of Cleveland.

Supported in part by the National Institute of Health, United States Public Health Service, The Elizabeth Severance Prentiss Foundation and Baxter Laboratories.

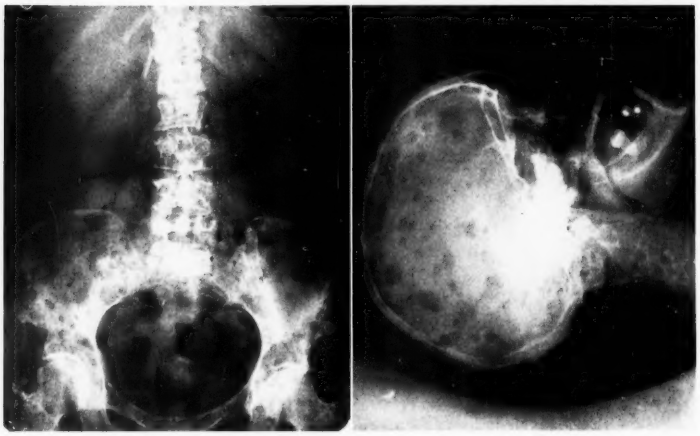

Fig. 1. Extensive osseous metastases in patient M.N.

mately 1 hour to complete the operation without technical difficulties. To date all patients have tolerated the procedure very well.

PREOPERATIVE AND POSTOPERATIVE MANAGEMENT

The schedule for adrenal substitution therapy has been briefly summarized in Table I. Fifty milligrams of cortisone are given orally at 12 and 6 p.m. on the day before surgery. Fifty milligrams of cortisone are given orally 1 hour before surgery and 100 milligrams intramuscularly one-half hour prior to surgery. Fifty milligrams of cortisone are then given intramuscularly every 4 hours the day of operation. Thereafter the amount is reduced progressively until a maintenance dose is established. As soon as the patient is able to take oral feedings the cortisone is given by mouth. The usual maintenance need of cortisone was found to be 25 milligrams, twice a day, although different patients received from 37½ to 75 milligrams daily in divided doses. Whenever these patients are subjected to added stress such as infection, injury, or further operations it is necessary to increase the cortisone dosage. Although Huggins and Dao have used desoxycorticosterone acetate in addition to the cortisone in the preoperative preparation and have also given extra sodium chloride in the diet, we have not found this necessary.

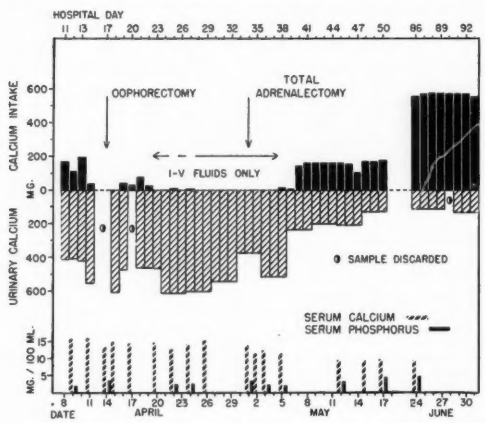
HOSPITAL DAY
11 13 17 20 23 26 29 32 35 38 41 44 47 50 86 89 92
OOPHORECTOMY
TOTAL ADRENALECTOMY
I-V FLUIDS ONLY
SAMPLE DISCARDED
SERUM CALCIUM
SERUM PHOSPHORUS
CALCIUM INTAKE MG.
URINARY CALCIUM MG. / 100 ML.
600 400 200 0 200 400 600
15 10 5
8 11 14 17 20 23 26 29 2 5 8 11 14 17 24 27 30
DATE
APRIL
MAY
JUNE

Fig. 2.* Urinary calcium excretion studies, patient M.N.

*Explanation of Figures 2, 3, and 4. The intake of various substances is indicated above the line. The output is shown below the line. The loss of various substances in the urine is indicated by oblique notched lines. Fecal nitrogen, sodium, and potassium are represented by the solid black areas below the line. The daily balance is indicated by the horizontal broken line.

Whole blood is given preoperatively to correct any anemia which may exist. Prior to operation 2 No. 18 needles or polyvinyl catheters are inserted in the antecubital or femoral veins for the administration of parenteral fluids. On the day of operation and the first postoperative day, 500 milliliters of 5 per cent dextrose in normal saline are given. Whole blood is administered in quantities to replace

TABLE 1.—THERAPY FOR TOTAL BILATERAL ADRENALECTOMY

Day	Amount of cortisone acetate, mgm.	Route of administration	Time
OR—1	50	Oral	12 Noon, 6 p.m.
Day of operation (q.4h.)	50 100 50	Oral IM IM	7 a.m. 8 a.m. 12 Noon, 4 p.m. 8 p.m., 12M, 4 a.m.
OR+1 (q.6h.)	50	IM	8 a.m., 2 p.m. 8 p.m., 2 a.m.
OR+2 (q.8h.)	50	IM	8 a.m., 4 p.m., 12 M.
OR+3 (q.12h.)	50	IM or oral	8 a.m., 8 p.m.
OR+4 (q.8h.)	25	IM or oral	8 a.m., 4 p.m., 12M.
OR+5 (q.12h.)	25	Oral	8 a.m., 8 p.m.

*Maintenance dose of cortisone acetate 25 to 50 milligrams daily, increased with stress. Blood, l-norepinephrine, carbohydrate and sodium chloride given as needed. Fluids 2,000 to 3,000 milliliters per day.

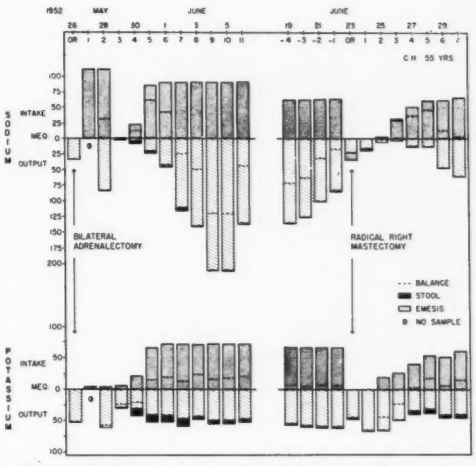

Fig. 3. Sodium and potassium balance studies, patient C.H.

sses which occurred at the time of operation. A continuous infusion of 5 or 10 per cent glucose is maintained during the day of operation and the first postoperative day, in order to avoid the development of hypoglycemia. A blood sugar level is obtained the afternoon of the day of surgery and repeated as often as necessary. Total fluid intake is kept at a maximum of from 2,500 to 3,000 milliliters for a 24 hour period because of the tendency of these patients to retain fluid. Although adequate amounts of blood, glucose, normal saline, and water are given so that hypovolemic, hypoglycemic, and hemorrhagic shock are avoided, periods of hypotension occur during the operation and for a varying period postoperatively. This is probably the result of vasodilatation associated with the removal of the adrenal medulla. This hypotension is rapidly corrected by the administration of l-norepinephrine. This is best done by mixing the norepinephrine in 5 per cent glucose (0.4 mgm. per 2,000 ml.) so that its administration can be titrated against the blood pressure.

At the time of surgery the patients are placed on constant uretheral drainage so that the hourly urine output may be measured. Since these patients are prone to develop postoperative ileus apparently due to the operative manipulation nothing is given by mouth until normal peristaltic sounds are heard or flatus is passed per rectum. If necessary, continuous gastric suction is employed. Ambulation is started on the day of operation.

The operation was well tolerated by all the patients and after the first few postoperative days, other than the administration of cortisone, they were managed in the same manner as any postoperative patient.

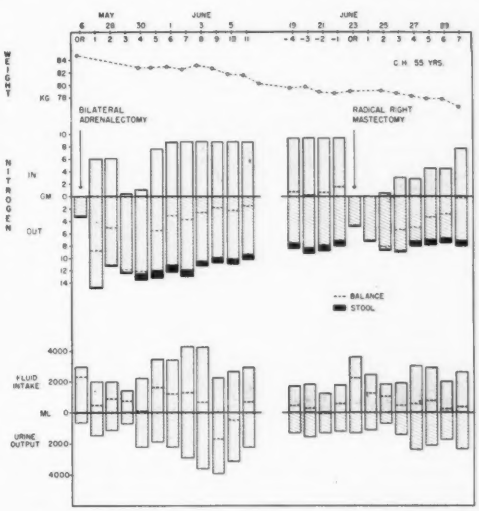

Fig. 4. Water and nitrogen balance studies, patient C.H.

METABOLIC STUDIES

Figure 1 illustrates the extensive osseous metastases present in patient M.N., a 54 year old white female. Because of extensive and rapid bone destruction, this patient exhibited a severe hypercalcemia associated with nausea, vomiting, anorexia, and chronic constipation which caused her to be bedridden for 2 months prior to admission.

Figure 2 illustrates the urinary calcium excretion studies made upon this patient. Because of her severe hypercalcemia it was considered dangerous to administer testosterone to this patient as this hormone increases the serum calcium level. Although the patient was several years postmenopause, bilateral oophorectomy was performed. Following bilateral oophorectomy, the patient remained in negative calcium balance with severe hypercalcemia. After bilateral adrenalectomy, urinary calcium levels fell progressively with a gradual return of serum calcium to normal levels. These changes were accompanied by dramatic clinical improvement. Within a few days following the procedure she was able to take a regular diet, had spontaneous bowel movements, and marked relief of bone pain. She was able to sit up in a chair in spite of multiple pathologic fractures. Two months after adrenalectomy, the patient was readmitted for metabolic studies. At this time, she was found to be in a positive calcium balance with a relatively normal calcium intake. Serum calcium levels remained normal after the fourth postoperative day. The reduction in urine calcium following bilateral adrenalectomy is thought to indicate a slowing or cessation of bone destruction by the metastases.

Figure 3 illustrates sodium and potassium balance studies in another patient. Approximately 1 month after bilateral adrenalectomy, a right mastectomy was performed on this patient in order to remove a sloughing necrotic tumor. It was noted that following both the adrenalectomy and radical mastectomy there was a period of sodium retention (positive balance) and increased potassium loss (negative balance). This is similar to the electrolyte changes which occur following any surgical procedure, and is the result of adrenal stimulation. In this patient it was due to the increased cortisone administration during and for several days following the operation.

Figure 4 illustrates nitrogen balance studies, water balance, and weight changes in the same patient. It was noted that after both procedures there was a temporary maintenance of weight in spite of a significant negative nitrogen balance. This may be explained by temporary retention of sodium and water as indicated in the fluid intake and output graph.

SUMMARY

Patients undergoing bilateral adrenalectomy for metastatic carcinoma of the breast demonstrate a temporary subjective improvement in their symptoms. Objective improvement is best demonstrated by correction of negative calcium balance and hypercalcemia. These changes persist for varying periods of time. Adrenalectomy had no demonstrable influence on the clinical course of the patient with melanosarcoma. Similar experience is reported by West and associates. Patients undergoing bilateral adrenalectomy showed profound metabolic changes which quickly revert to the normal status under adequate cortisone therapy.

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CONSTRUCTION AND RECONSTRUCTION OF THE VAGINA

HERBERT CONWAY, M.D., F.A.C.S., and RICHARD B. STARK, M.D., F.A.C.S.,
New York, New York

ABSENCE of the vagina, whether congenital or due to trauma, is a condition which occurs rarely. It has been estimated that congenital agenesis of the vagina occurs about once in four thousand births. Whitacre and Chen reported that cicatricial closure of the vagina occurs occasionally in China following instillation of corrosive substances into the vagina in the treatment of dysmenorrhea. It is difficult to estimate the number of patients with postoperative or posttraumatic absence of the vagina, although this number is increasing with the wider application of radical pelvic surgery for neoplasm.

A patient with congenital agenesis of the vagina usually is oblivious to her condition until puberty when she may be examined because of amenorrhea. She may remain unaware of it until she is married and discovers that coitus is impossible. Severe mental depression may result when the patient discovers her anomaly.

Embryologically, agenesis of the vagina occurs because of failure of the uterovaginal process to progress from the solid to the hollow form. It is a condition of retention of the solid vaginal form. Normally, the anlage of the portio vaginalis is defined between the third to the sixth month of intrauterine life. Following the formation of the anlage for the two vaginal fornices, the vagina becomes hollow. The vaginal lumen appears normally in an embryo that has grown to a trunk length of 150 to 200 millimeters. Agenesis of the vagina is often associated with atrophic, infantile, or bicornate uterus, and occasionally with rectovesical or rectoperineal fistula. Ovaries are normal. Usually the secondary sexual characteristics are well developed in patients with agenesis of the vagina. The labia and the clitoris are normal, but the vaginal dimple (usually present) gives the appearance of an imperforate hymen. About 25 per cent of patients with vaginal agenesis have associated major anomalies of the urinary tract. It is well to consider the possibility of the presence of a pelvic kidney if a palpable lower abdominal mass is associated with vaginal agenesis.

As is true with all congenital anomalies, the specific etiology remains obscure, but viral infection, riboflavin deficiency, vitamin A deficiency, transient hypoxia, pelvic irradiation, and the administration of corticotropin or cortisone during pregnancy may result in an anomalous birth. Search of the literature reveals no report in which congenital absence of the vagina occurred in successive generations. Therefore heredity appears not to play a role in the causation of this anomaly.

Pelvic trauma has resulted in obliteration of the vagina by scar following forceps delivery (gynatresia). Thermal and lye burns are reported to have caused scarring and stenosis. An increase in the number of patients undergoing pelvic exenteration for extensive malignant tumor has increased the number in whom the vagina is absent as a result of radical surgery. Some of these patients are yet in an age group in which mention of the possibility of later reconstruction of the vagina might allay their natural apprehension over the radical nature of the proposed curative surgery.

HISTORY

Since this anomaly (agenesis of the vagina) was first described by Realdus Columbus in 1573, many methods have been devised for constructing a vagina or for reconstructing the patency of the vagina. Not all of the procedures described by surgeons have been rewarded with success. Among the methods used to construct the vagina are the following:

From the Department of Plastic Surgery, The New York Hospital-Cornell Medical Center. This work aided by a grant from The Vincent Astor Foundation.

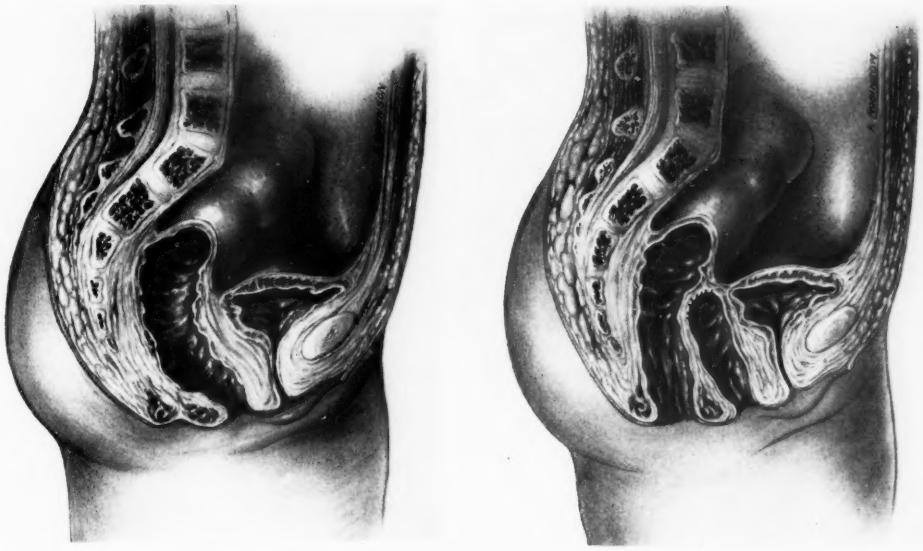
Fig. 1. Cases 1, 2, 3. A vaginal canal is dissected bluntly between the bladder and the rectum for a depth of 11 to 13 centimeters. A urethral sound in the bladder and a finger in the rectum help to identify the boundaries of these structures. A free graft of thick-split skin is glued to an obturator of dental compound. The obturator may be removed after the seventh day and replaced by a lighter one made of balsa wood and covered with a condom, which, after complete epithelialization has occurred, is worn only at night.

(a) free grafts of skin, of mucous membrane or of fetal membrane; (b) pedicle flaps of skin and subcutaneous tissue taken from the thighs; (c) the insertion of obturators (made of sponge, balsa wood, lucite, glass, pyrex, rubber, bakelite, acrylic, or metal) without coverage by graft and (d) pedicles of ileum, sigmoid, rectum, peritoneum, or hernia sac.

Dupuytren (1817) is credited with having made the first surgical attempt to construct an artificial vagina. Pedicle flaps from the inner thigh and labia were used by Heppner in 1872 in attempted construction of the vagina. This method was used successfully by Beck in 1900. Graves devised a similar procedure in 1908. Sneguireff (1904) first used the rectum to construct a vagina. He utilized a sigmoidal "pull-down" to form a perineal colostomy. Popow (1910) and Schubert (1914) also used the rectum to form a vagina. Use of the sigmoid to construct an artificial vagina was suggested by Baldwin in 1904. In 1907 he transferred a double loop of ileum for this purpose. A mortality rate estimated variously from 6 to 25 per cent attended this last procedure in the hands of other surgeons. The use of free thick-split grafts of skin was first described by Abbe in 1898 and was popularized later by Counseller and by McIndoe. Wharton (19) utilized an uncovered obturator without epithelium to maintain the form of the vagina, allowing the cavity to epithelialize spontaneously, but he later used thick-split grafts over an obturator (21). Owens and Adams advocated the use of free grafts of skin wrapped about obturators. Again, Wharton (20) reported a case in which a balsa wood obturator perforated the rectovaginal septum 5 weeks postoperatively. Campbell, Frank (8), and Steinmetz advocated the persistent indentation of graduated pyrex forms as a means of creating a cul-de-sac to serve as a vagina. Wharton cites a case of Kelly's in which a vagina had been made solely by phallic penetration (21). Frank and Geist (9) devised a method of vaginal construction which utilized a tubed pedicle formed upon the medial thigh. This was inverted at a later operative stage and inserted into the newly dissected cul-de-sac. Flynn and Duckett have collected 8 such constructions and added 1 case of their own.

The optimum time for surgical intervention is prior to a contemplated marriage when regular dilation by intercourse is in prospect. It is wise to reserve the operation for women who will use their constructed vagina. It is interesting to note that Wharton reported the formation of a vagina in a male pseudohermaphrodite who had been raised as a female.

Although there have been hearsay reports of successful conception following construction of the vagina for agenesis, the coexistence of vaginal, uterine, and tubal anomalies makes this eventuality unlikely. J. S. Davis epitomized the indications for construction of the vagina by saying, "In the great majority of cases, the new vagina is constructed to prevent marital unhappiness or mental instability in the patient."



a b

Fig. 2. Case 4. a, This patient presented herself with a congenital absence of the vagina, an imperforate anus, and a rectoperineal fistula. b, The rectosigmoid was divided 5 inches proximal to the anal sphincter, and the distal segment was closed, forming a cul-de-sac lined with mucous membrane which substituted for a vagina. A "pull-down" procedure anastomosed the sigmoid to the anal dimple so that function of the sphincters was preserved.

AUTHORS' CASES

In this presentation 5 patients are listed in whom 3 different types of vaginal construction or reconstruction have been employed. Three patients were operated upon for congenital agenesis of the vagina using thick-split grafts of skin over an obturator. In 1 of these, a nubbin of vaginal pouch was found attached to the cervix of an infantile uterus. The vagina was constructed by inlay graft of skin which was sutured to the rudimentary vaginal stump. This operation was done 6 years ago when the child was 8 years old, and menstruation has not yet occurred. In a fourth patient, the vaginal construction for agenesis was performed using the rectum as a vagina, by a technique similar to that reported in 1904 by Sneguireff, but with preservation of the rectal sphinters at the point of anal sigmoidostomy. In the fifth case (a patient who previously had been treated by pelvic irradiation and radical pelvic surgery) vaginal reconstruction was achieved by using pedicle flaps from the thighs. In this patient the flap technique was utilized because of the dense postoperative pelvic fibrosis, a state which was looked upon as unfavorable for the persistence of cavity formation by inlay graft.

Case 1. N.Y.H. No. 637264. This 20 year old white, single secretary[1] entered The New York Hospital because of amenorrhea which had been present all of the patient's life. She was moderately obese with small breasts but normal labia and a vaginal introitus which admitted the tip of an examining finger. Examination under anesthesia failed to reveal a vagina. Rectally, what appeared to be a cervix could be palpated, but no fundus or adnexa could be outlined.

Construction of the vagina with a free graft of thick-split skin wrapped about an obturator was performed. Eleven days following surgery, the obturator of dental compound was removed and replaced with one of balsa wood covered with a condom. The graft was observed to have been nearly completely successful. Granulations were cauterized upon several occasions with silver nitrate. A completely epithelialized vaginal vault of 11 centimeters was obtained and has been maintained by the perseverance of the patient who has worn her obturator steadfastly at night. She has had intercourse since.

[1]This was a patient of Dr. Charles M. McLane, New York, New York, in association with whom the operation was performed.

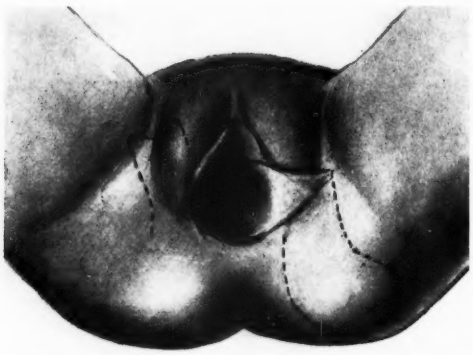


Fig. 3. Case 5. This patient had been treated previously by pelvic irradiation and radical pelvic surgery for carcinoma of the cervix. Because of the presence of dense scar in the perineum, gluteal and thigh pedicle flaps were turned into the vaginal canal which had been formed by dissection.

CASE 2. N.Y.H. No. 582660. This 22 year old white, married woman[1] entered the hospital for construction of a vaginal canal. Shortly after her marriage, 4 months before hospitalization, the patient found that coitus was impossible. She sought medical aid and was admitted to another hospital for hymenotomy. Following an unsuccessful procedure the patient was informed that she had no vagina. The patient then entered The New York Hospital. The patient was an attractive young female with well developed secondary sex characteristics. The labia and the vaginal introitus were normal, but only the tip of an examining finger could be admitted into a dimple which was at the location of the vaginal introitus in the normal subject. Under anesthesia two small ovaries could be palpated in either lateral pelvic region, but no uterine fundus could be felt. At operation, a vaginal canal was dissected between the bladder and the rectum. To guide the dissection a urethral sound was placed in the bladder and an examining finger in the rectum. A thick-split graft of skin was taken from the lower abdominal wall, above the pubic hairline so as not to transplant hair follicles. A cast of the vaginal canal was made of dental compound which remains semisolid while warm, but becomes solid and firm as it cools. Using this cast as an obturator, the graft was wrapped about and glued to the obturator. The free margins of the graft were sutured together so that the entire obturator was covered by graft. Graft and obturator were then inserted into the vaginal canal. They were held in situ by suturing the labia together and applying a perineal pad and T-binder. The obturator was removed upon the seventh postoperative day when it was apparent that the cavity was epithelialized almost completely. In two small areas the graft was unsuccessful. No attempt was made to surface these areas with additional grafts of skin. The granulations were cauterized with silver nitrate periodically, and the patient continued to wear a lighter obturator made of balsa wood covered with a condom. She was discharged upon her fourteenth postoperative day. Intercourse was begun 7 weeks following surgery. The patient experienced normal orgasms from the inception of intercourse. This patient has been in the clinic regularly for 2 years. She has a vaginal canal measuring 10 centimeters in depth at the present time. The skin graft has developed the appearance of mucous membrane.

CASE 3. N.Y.H. No. 452826. This 8 year old white girl was first admitted to The New York Hospital in August, 1946, because of precocious puberty which had occurred from the age of 2 years. She was found on examination to have complete congenital vaginal atresia. Exploratory operations revealed normal adrenals, a normal uterus, fallopian tubes, ovaries. Biopsy of the adrenal glands showed that these were normal.

This patient was readmitted to The New York Hospital in 1947 for construction of the vagina using a free thick-split skin graft over an obturator. It was in this case that the graft was sutured to a rudimentary vaginal pouch. At the age of 14 the patient had not yet menstruated. She made an uneventful recovery and was discharged wearing an artificial dilator. In the ensuing months she developed a stricture at the vaginal introitus where several granulating areas were present. Accordingly, she was operated upon again and a split-thickness skin graft was applied to this area. This graft was completely successful, and she was again fitted with an obturator made of acrylic. The progress of this patient has been entirely satisfactory. When she was last seen in the plastic surgery clinic in December, 1952, the vaginal depth was 12 centimeters.

CASE 4. Bellevue Hospital No. 44748-51. This 19 year old Puerto Rican girl was admitted to the Second Surgical Division (Cornell), Bellevue Hospital, in July of 1951, because of absence of the vagina and anus. She had a perineal anus, but the normal anal dimple was located posteriorly where intact sphincters could be demonstrated upon stimulation. Defecation was ill-controlled. The examining finger revealed a narrow sinus from the outlet to a depth of 5 centimeters. The sinus connected with a rectal vault. This then was a case of congenital absence of the vagina with imperforate anus but with defecation by perineal fistula. Her secondary sex characteristics were normally developed.

An exploratory laparotomy revealed her ovaries to be normal. There was only a rudimentary fallopian tube on the left, and no uterus, cervix, or vagina were found. The rectosigmoid was divided 5 inches above the fecal orifice. The distal segment was closed and suspended from the abdominal wall to form a cul-de-sac lined with mucosa in substitution for a vagina. A "pull-down" procedure was utilized whereby the proximal sigmoid was anastomosed to the anal dimple so that function of the sphincters

[1]This operation was performed in association with Dr. Richard Morrison, now of San Mateo, California.

could be preserved. The patient has had control of bowel movements through newly formed rectum but has not attempted to use her vagina.

CASE 5. N.Y.H. No. 502048. This 40 year old colored female was admitted to The New York Hospital in March, 1948, when a diagnosis of squamous cell carcinoma of the cervix was made. She was treated with x-ray and radium. However, in November of 1948, pelvic exenteration with a total hysterectomy, bilateral salpingo-oophorectomy, cystectomy, and abdominal-perineal resection was performed. Ureterosigmoidal transplants were done, leaving her with a wet, abdominal colostomy. The patient had an uneventful recovery.

She was readmitted to the hospital in September, 1950, for plastic reconstruction of the vagina, as she had been unable to have intercourse with her husband. Physical examination was within normal limits. The colostomy in the midline scar of the lower abdomen functioned well. There was a well healed scar in the perineum with only rudimentary labia minora remaining anteriorly. Since the vagina had been scarred by irradiation and surgery, full thickness flaps from the left gluteal region and right inner thigh were employed to construct the vagina. The artist's sketch shows the areas from which the flaps were elevated (dotted lines) and the flaps rotated to their positions to line the constructed vaginal vault. The vagina measured 6 centimeters in depth. Her postoperative course was uneventful, and she was discharged on the 26th postoperative day with instructions to make daily use of an obturator for autodilatation of the new vagina. She has been seen on many occasions, but has never attempted to use the vagina, and has been lax in her attempts at autodilatation. Considerable scar retraction has developed which has diminished the size of the vagina.

CONSTRUCTION OF VAGINA BY FREE GRAFT OF SKIN

It is held generally that the simplest surgical technique for the formation of a vagina is also the safest. The simplest procedure involves the use of a free thick-split graft of skin which is wrapped about an obturator. The blunt dissection of the vaginal canal is accomplished easily in the plane between the urinary bladder and the rectum. Dissection is carried to a depth of 11 to 13 centimeters. A urethral sound in the bladder and a finger in the rectum help to identify the boundaries of these structures. Complete hemostasis is imperative if the graft is to succeed. A free graft of thick-split skin (cut at .018 to .022 inch) contains sufficient dermis to afford resiliency. Hence, the likelihood of contraction of the graft is lessened. For intimate contact of the graft to the concavity, an obturator of dental compound is ideal. The cutaneous surface of the graft is glued to the obturator of dental compound and its margins sutured to each other with fine catgut. This temporary obturator is removed on the seventh postoperative day and is replaced then by a light obturator fashioned of balsa wood, covered with a condom. If the thick-split skin graft fails to take in a few small areas, granulations which form in these sites should be cauterized by silver nitrate to facilitate epithelialization. It is well to constipate the patient in the immediate postoperative period to limit fecal contamination. However, infection is encountered rarely in these cases. An indwelling catheter may be utilized for the first week postoperatively. The continuous use of a rigid obturator in the postoperative period may lead to perforation into the rectum. The light weight of balsa wood makes it preferable to other materials for use as obturators. After the vault of the vagina is completely epithelialized, the obturator should be worn during sleep only. The obturator exerts less pressure upon the rectal septum when the patient is recumbent than when sitting. Coitus should be encouraged in the married patient after epithelialization is completed as it constitutes the best means of dilatation by which to guard against contraction and reduction in the capacity of the vagina. The vaginal outline after operation can be demonstrated by x-ray examination after coating the obturator or filling a condom with barium. Miller and his associates have found from vaginal smears that skin transplanted to the vagina undergoes the same cyclical changes as vaginal mucosa.

Results following the use of free thick-split grafts of skin have been eminently satisfactory in 2 cases. In the third case, cicatricial annular contracture of the introitus complicated an otherwise good result. This patient is still under treatment for the introital stenosis. In this patient the thick-split grafts were anastomosed to a rudimentary blind vaginal pouch. The patient in whom the rectum was used to form a vagina has maintained patency of the vaginal vault. Intercourse has not been attempted. The operative result was disap-

pointing in the case in which reconstruction of the vagina followed heavy pelvic irradiation and radical pelvic surgery. In that case, pedicle flaps from the thighs were turned into the newly formed cul-de-sac, but pelvic cicatrix diminished the size of the vaginal concavity and finally obliterated it. This patient did not co-operate in wearing the vaginal obturator after operation and did not attempt intercourse.

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BETA-GLUCURONIDASE STUDIES IN WOMEN

VI. Premenopausal Vaginal Fluid Values in Relation to Invasive Cervical Cancer

S. CHARLES KASDON, M.D., F.A.C.S., F. HOMBURGER, M.D., E. YORSHIS, B.S., and WILLIAM H. FISHMAN, Ph.D., Boston, Massachusetts

THE common presenting sign of early cancer of the cervix is irregular vaginal bleeding and staining. In the postmenopausal woman vaginal bleeding of any degree is an arresting sign. In contrast, in the premenopausal woman, genital tract bleeding is open to many explanations, most frequently of a benign significance. For this reason, the clinical diagnosis of cancer of the cervix before the menopause is difficult. Phenomena related to cancer which are amenable to quantitative measurement deserve study, particularly in this group of women. Promise of useful diagnostic information has been forthcoming from this laboratory in a series of publications dealing with "β-glucuronidase" phenomena in women.

This paper represents the continuation of studies first reported in 1950 concerning the factors (physiologic and pathologic) which influence vaginal fluid β-glucuronidase activity. Base line studies were completed to provide tentative working standards of enzyme activity in relation to ovarian function (age, menopause, and castration)(3). Thus, vaginal β-glucuronidase activity was more frequently elevated above a chosen value in postmenopausal subjects and in ovariectomized women. The factors of enzyme-rich vaginal leucocytes (6) or of Trichomonas vaginalis organisms (5) appeared unimportant in explaining significantly elevated β-glucuronidase levels in vaginal fluid. It was found that at midmenstrual cycle a low range of vaginal fluid β-glucuronidase activity occurs (2). In cancer of the cervix, consistently high β-glucuronidase activity has been observed in the tumor tissue when compared to the benign adjacent tissues (4).

In vaginal fluid taken from premenopausal subjects, significantly high values were found in the majority of these patients when cancer of the cervix was present. In contrast, healthy postmenopausal women frequently exhibit high values and the explanation of these levels appears more complex. Accordingly, for the present, attention has been directed toward the study of vaginal β-glucuronidase in premenopausal women in relation to cancer of the cervix.

In this report, 386 noncancerous premenopausal women have been investigated with respect to their vaginal fluid β-glucuronidase activities. The present findings confirmed the data reported in a previous series of control subjects. In addition, the high values encountered were usually correlated with clinical conditions such as vaginitis, invasive cervical cancer, and ovarian dysfunction. The data concerning preinvasive cancer will be reported separately.

PLAN OF STUDY

The majority of the subjects in this study were presumably healthy premenopausal women who were undergoing a routine periodic physical examination at the New England Medical Center. Others were studied at the Gynecology Clinic of the Boston Dispensary. In view of the frequency of low vaginal fluid β-glucuronidase values at midmenstrual cycle, a great many observations were concentrated at this phase of the menstrual cycle. It was hoped in this way to reduce the varia-

From the Cancer Research and Cancer Control Unit, Departments of Surgery, Medicine, and Biochemistry, Tufts College Medical School, Boston, Massachusetts.

This work was supported by grants-in-aid from the National Cancer Institute of the National Institutes of Health, United States Public Health Service, Bethesda, Maryland, and by an Institutional Grant of the American Cancer Society, Inc., New York, New York.

TABLE I.—VAGINAL FLUID β-GLUCURONIDASE IN PREMENOPAUSAL WOMEN WITHOUT CLINICAL CERVICAL CANCER

	Subjects with fluid assay under 300 u/g†		80 per cent value* u/g
	No. of subjects	Per cent	
Total 1950 controls	288	80.6	300
Total 1952 controls	386	84.0,	200–300
1952 control subjects studied in the first two-thirds of the menstrual cycle	340	86.5	200

*80 per cent value, has been defined as the "level below which 80 per cent of women in the . . . group are found."
†u/g is units per gram.

tion due to ovarian function. Most of the patients with cancer of the cervix were studied in the Tumor and Gynecology Clinics of the Boston Dispensary. In these, the diagnosis of cancer was based on histologic evidence in every case.

The vaginal fluid specimens were secured by means of a Papanicolaou pipette in a standard fashion described previously (3). Smears were prepared for cytologic examination and a weighted aliquot of the material was assayed for β-glucuronidase activity as described (3).

RESULTS

In Table I, a comparison has been made of data on vaginal fluid β-glucuronidase collected from two successive series of controls. It should be noted that the 1952 data include a higher proportion of premenopausal women in the first two-thirds of the menstrual cycle than did the 1950 series (see previous discussion). Inspection of the table indicates close agreement in the two sets of data. In the last third of the cycle 76 per cent of 46 subjects assayed less than 300 units per gram of vaginal fluid, the "80 per cent value" being 300 units per gram. A total of over 1,300 vaginal fluid specimens were assayed.

TABLE II.—COMPARISON OF VAGINAL FLUID β-GLUCURONIDASE VALUES IN 2 SERIES OF CONTROL STUDIES IN 674 PREMENOPAUSAL AND IN 318 POSTMENOPAUSAL WOMEN

	β-glucuronidase					
Series	Total No. of subjects	u/g below 300		u/g above 300		80 per cent value u/g
		No.	Per cent	No.	Per cent	
Premenopause						
1950	288	232	80.6	56	19.4	250–300
1952	386	324	84.0	62	16.0	200–250
Postmenopause						
1950	212	119	56.0	93	44	750–800
1952	106	66	62.0	40	38	450–500

A composite picture of vaginal fluid β-glucuronidase in 992 women is illustrated in Table II. It shows that there is a preponderance of low vaginal fluid β-glucuronidase values in women who have not yet reached the menopause. Only 17 per cent of these subjects exhibit values higher than 300 units per gram.

In Table III data on hysterectomized women are tabulated comprising all our observations to date. Essentially the same results are now found as were reported in 1950.

The vaginal fluid β-glucuronidase data obtained from *premenopausal* subjects with invasive epidermoid cancer of the cervix are presented in Table IV. Thirteen out of these 16 patients exhibited elevated vaginal fluid β-glucuronidase activities.

In Figure 1 is presented the percentage incidence of elevated vaginal fluid β-glucuronidase in two different populations of women, one consisting of apparently healthy subjects undergoing a routine physical examination and the other, a group of women seen in a gynecology outpatient clinic.

DISCUSSION

The establishment of reliable standard values in healthy women is a prerequisite for the intelligent interpretation of vaginal fluid β-glucuronidase phenomena. Accordingly, in 1950, tentative standards were defined, based on observations made in 500 women without genital cancer. In order to arrive at accepted values for nonmalignant states, a second series of approximately 500 women have been studied and a comparison has been made with the first group. It was found that agreement was surprisingly good in the normal constants arrived at in both series of women, and it is, therefore, considered safe to advance numerical normal values for vaginal fluid β-glucu-

ronidase which have a secure statistical basis in evaluating certain gynecologic disorders.

In the past, 300 units of β-glucuronidase per gram of vaginal fluid was arbitrarily selected as a level to separate normal from abnormal values. This level corresponded to the "80 per cent value" previously defined. Now, in the light of accumulated experience with many control subjects and a sizable number of patients with cervical cancer, we consider it justifiable to differentiate between normal and abnormal states at 400 units β-glucuronidase per gram. By doing so, almost 90 per cent of premenopausal women without cervical cancer are found to be in the normal category (Table V).

From the study of 16 premenopausal women with invasive epidermoid cancer of the cervix, 13 were found to exhibit vaginal fluid β-glucuronidase activities above 400 units per gram (20 out of 25 observations). The elevated values in the range of 400 to 1,500 units per gram were closely concentrated when compared to the spread of high values observed in the noncancer control groups.

In this laboratory, on the basis of the data presented, the following criteria are now employed routinely in classifying premenopausal women by means of vaginal fluid β-glucuronidase. Group I, values below 300 units per gram, *normal;* Group II, values between 300 and 400 units per gram, *suggestive;* Group III, values above 400 units per gram, *abnormal.*

Group I—Normal. Accumulated experience with some 700 normal and healthy premenopausal women has demonstrated that 85 per cent of these exhibit β-glucuronidase vaginal fluid values below 300 units per gram. This then is the basis for calling this group normal. In the present study, it was possible to compare the range of values obtained in a group of women undergoing routine health examinations in the Health Protection Clinic as opposed to another group who were outpatients at the Gynecology Clinic. It is clear from Figure 1 that more women in the Health Clinic were classified in Group I than was the case for women seen in the Gynecology Clinic.

Although a low vaginal fluid β-glucuronidase value may be found in pathologic conditions such as trichomonas and other vaginitides and occasionally in cancer of the genital tract, for most practical purposes it is regarded as having a benign significance. On the other hand, the occurrence of a low value in a patient with cancer should be no more disturbing than the occasional failures which are encountered in any laboratory diagnostic procedure. Thus, repeated assays are indicated as well as most careful attention to technique before a conclusion is reached.

TABLE III.—RELATIONSHIP BETWEEN β-GLUCURONIDASE ACTIVITY IN THE VAGINAL FLUID AND HYSTERECTOMY

β-glucuronidase values u/g	Type of hysterectomy					
	Supracervical		Panhysterectomy		Type undetermined	
	No. observ.	Per cent	No. observ.	Per cent	No. observ.	Per cent
Below 300	39	73	20	42	17	74
Above 300	14	27	28	58	6	26

TABLE IV.—VAGINAL FLUID β-GLUCURONIDASE IN PREMENOPAUSAL WOMEN WITH INVASIVE EPIDERMOID CANCER OF CERVIX

Patient	Age, years	Extent of lesion (League of Nations)	Duration of symptoms	Vaginal β-glucur. u/g
1952 Series				
E.F.E.	49	I	2 wks.	999
B.S.	48	III	6 mos.	1442
G.C.	39	I	No symptoms	45
N.R.	35	II	6 wks.	935
M.H.	31	III–IV	1 yr.	890
H.G.	46	II–III	—	140
1950 Series				
R.D.	36	I–II	7 mos.	474, 525
W.A.	32	I	2 yr.	1045
R.C.	30	II–III	4 mos.	857
P.L.	44	II	—	784, 715
N.M.	49	III	2 yr.	1145, 1600
F.M.	40	III	6 wks.	645, 755, 925, 580
M.M.	42	IV	—	259, 430, 649, 349
M.G.	48	I	No symptoms	1105
B.M.	32	II–III	—	490
S.B.	35	I	—	173

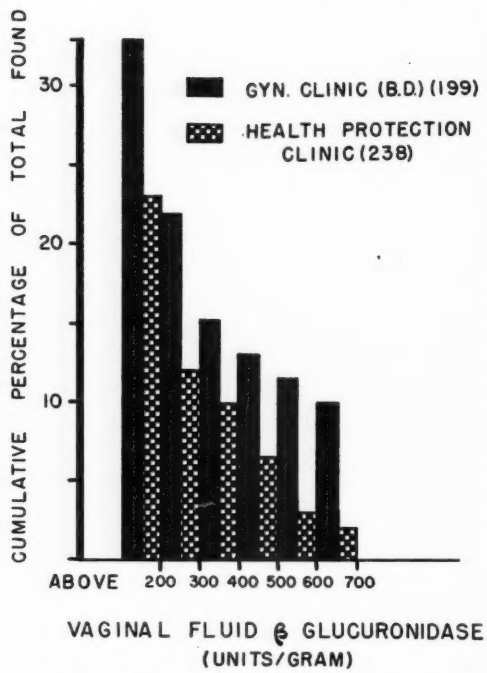

Fig. 1. Incidence of abnormal values in premenopausal women.

In our experience the most consistent and reproducible values are obtained when the specimens are collected in the first two-thirds (up to the seventeenth day) of the menstrual cycle.

Group II—Suggestive. A small number of subjects (5 per cent) exhibit values between 300 and 400 units per gram. At the present time, this group is not given special emphasis but is intended to bridge the gap between normal and abnormal values. In the study of the relationship between the menstrual cycle and the vaginal fluid β-glucuronidase, occasionally values in this range were encountered. There is no reason *a priori* to attach undue importance to a value in this range. On the other hand, an occasional patient with cervical cancer exhibits low values in this range and below.

TABLE V.—SUMMARY OF SIGNIFICANT DATA IN PREMENOPAUSAL WOMEN

Total No.	Subjects	Vag. fluid β-glucuronidase u/g			
		Below 400		Above 400	
		No.	Per cent	No.	Per cent
386	No cancer of uterine cervix	342	88.6	44	11.4
16	Untreated primary cancer of uterine cervix	3	18.8	13	81.2

Although there were many exceptions, a tendency did exist for a positive correlation between the leucocyte population and the vaginal fluid β-glucuronidase going from Group I to Group II (6). One may, therefore, expect to find a higher incidence of inflammatory disorders in this group.

Group III—Abnormal. The reasons for considering values above 400 units per gram as abnormal are as follows: (a) it is in this group that one encounters the majority of premenopausal women with cancer of the cervix; (b) in addition, there is a preponderance of preinvasive cancer and atypical nuclear changes in the cytologic preparations of cervical and vaginal smears (1); (c) on the basis of the known dependence of vaginal fluid β-glucuronidase on the level of ovarian activity, in the absence of cervical cancer, ovarian failure is closely correlated with abnormally elevated values. Taken alone, a Group III value may either be abnormal within physiologic limits or it may have pathologic or neoplastic significance. It is obvious that a critical appraisal of such a value requires systematic investigation by techniques of cytology, pathology, and bacteriology.

At the present time, the following routine is recommended in investigating an abnormal vaginal fluid Group III β-glucuronidase value in premenopausal women: (1) Repeat the enzyme assay on another fresh vaginal fluid specimen. (2) Cervical and vaginal cytologic smears are prepared and carefully interpreted. (3) Cervical tissue biopsies are secured and studied pathologically. (4) Bacteriologic and parasitologic investigation is made on fresh specimens of vaginal fluid. (5) Evaluation is made of the subject's endocrine balance.

When step 2 or 3 of this routine reveals the presence of malignant disease, the clinical

management is clear. In the absence of malignant disease based on these two criteria, all other gynecologic disease should be actively treated and the enzyme assays repeated after these conditions have been ameliorated. Should the enzyme values subsequently remain in Group III, periodic repetition of the routine outlined is indicated.

The major practical advantage of β-glucuronidase assay of vaginal fluid is considered to be the ability to segregate by a single chemical procedure those premenopausal women in whom there is a high probability of serious gynecologic disease. These women may then be profitably investigated by the recognized established clinical routines with a minimum of wasted effort and economic loss.

Obviously, the more specimens of vaginal fluid assayed in a given patient, the smaller the possibility of failure to detect the cancer suspects.

SUMMARY

1. In a control study comprising approximately 1,300 observations in 386 premenopausal women, 88.6 per cent were found in the normal category of vaginal fluid β-glucuronidase activity (under 400 units/gram).

2. Of 16 premenopausal women with untreated primary cancer of the uterine cervix, 13 (81 per cent) were in the abnormal category of vaginal fluid β-glucuronidase activity (above 400 units/gram).

3. On the basis of these biochemical findings together with the disciplines of pathology and cytology, a routine is proposed for the clinical evaluation of abnormal vaginal fluid β-glucuronidase values.

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CYSTECTOMY FOR CARCINOMA OF THE URINARY BLADDER

FREDERICK A. LLOYD, M.D., Chicago, Illinois, and
GEORGE BAUMRUCKER, M.D., Hinsdale, Illinois

THE treatment of carcinoma of the urinary bladder has been a discouraging chapter in the field of urology. As long as surgery has been the most successful method of controlling cancer, early and wide excision of the neoplasm has been the desired goal. Wherever possible, removal of the entire involved organ with the surrounding adipose tissue and local lymph nodes was the method of choice. In the case of the urinary bladder complete excision included removal of the prostate and seminal vesicles. Diversion of the urine was also necessary.

Early attempts at cystectomy carried with them an alarming immediate mortality, partly due to technical difficulties and also as a result of implantation of the ureters into the bacteria-laden bowel. The method was, therefore, temporarily abandoned. The more conservative methods of treatment, especially local excision and electrocoagulation, either transurethrally or through the open bladder subsequently enjoyed wide popularity. Judged by fundamental standards they were unsurgical. Few cases were permanently cured. But the relative ease of their performance, and the fact that the tumor was temporarily controlled seemed to justify their employment. Even though repeated treatments were often necessary, many patients lived relatively comfortable and useful lives for long periods of time. The length of hospitalization was within reasonable limits, the postoperative comfort was satisfactory, and the economic drain upon the patient was not too great.

During the past decade, largely as a result of improvement in surgical techniques and after-care, cystectomy has again enjoyed wide popularity. The improvement of the technique of cystectomy by Hinman, Higgins, Millin, Couvelaire, Ferris, Priestley, and others, and of the technique of ureterosigmoidostomy by Jewett, Hinman, Weyrauch, Schinagel, Flocks, Leadbetter, Nesbit, Cordonnier, and many other investigators, too numerous to mention, have placed the total operation within the reach of every competent operator. Preoperative bowel sterilization with modern agents has assured the healing of the implant and almost eliminated the immediate threat of postoperative pyelonephritis. A better understanding of fluid and electrolyte balance and the liberal use of blood transfusion have also helped to reduce the immediate mortality of the total operation to reasonable levels. Leadbetter and others have sought to improve the ultimate cure rate by wide removal en bloc of the pelvic adipose tissue and local lymph nodes.

Unfortunately most of the publications have concerned themselves mainly with operative technique and immediate results. Statistics as to 5 and 10 year survivals have been far too infrequent. Little is mentioned as to length of hospitalization, the general postoperative comfort of the patient, his emotional adjustment to his situation, and the complications which might occur. Recently Colby has demonstrated how poorly the long term survivals after cystectomy compare with those of cases treated by more conservative measures.

REVIEW OF PERSONAL CASES

At the Hines Hospital we have treated 402 cases of carcinoma of the urinary bladder from 1945 to 1952. During this period we performed 50 cystectomies and carried out diversion of the urine without removing the bladder in an additional 36. This series is far too small for an accurate statistical analysis, especially since so many factors were involved. Some of these cases were also too recent for a 5 year

From the Department of Urology, Veterans Administration Hospital, Hines, Illinois.

follow-up. We do believe, however, that an objective appraisal of the results at this time may be of some value.

Thirty-eight patients, 76 per cent, have died: 29 during the first year, 3 the second year, 3 the third year, 1 the fourth year, and 2 the fifth year (Fig. 1). The greatest mortality was in the first year (76 per cent). Ninety per cent of the fatal cases succumbed within 3 years.[1]

Twelve patients are still alive: 1 for 0 to 1 year, 4 for 1 to 2 years, 3 for 2 to 3 years, 1 for 4 to 5 years, and 3 for 5 to 6 years.

Twenty-six of the 50 patients, or 52 per cent, had demonstrable preoperative damage to the upper urinary tract. Four of these are still alive. Of the 24 patients without such damage 8 are still alive. That previous damage to the upper tract adversely affects the outcome is obvious. Figure 2 shows the comparative longevity of the fatal cases. There is not too great a difference between the two curves. This is due to the fact that the safer ureterocutaneous implant was employed in patients with more advanced upper tract damage and the more hazardous ureterosigmoid implant in those with less serious damage. If the same method of urinary diversion had been used in all cases there would have been a greater spread between the two curves.

That ureterocutaneous implantation was safer than ureterosigmoid anastomosis in the presence of upper urinary tract damage is shown in Figure 3. Here too the difference is greater than the curves would imply, because the more hazardous ureterosigmoid implant was used only in the patients with less serious upper tract damage.

So far in this series there have been 6 long term survivors (4 to 6 years). The bladders were soft on rectal palpation under anesthesia in all of these, and subsequent pathologic examination of the excised bladders revealed either no involvement or only superficial infiltration of the muscular wall. Two patients have, nevertheless, since died of metastases (Table I).

In 14 of the patients who returned to the hospital to die autopsy was obtained. In 10 pyelonephritis was demonstrable, and 5 had metastases.

[1]In interpreting these graphs, lest the mortality seem too high, it should be kept in mind that only the fatal cases are included.

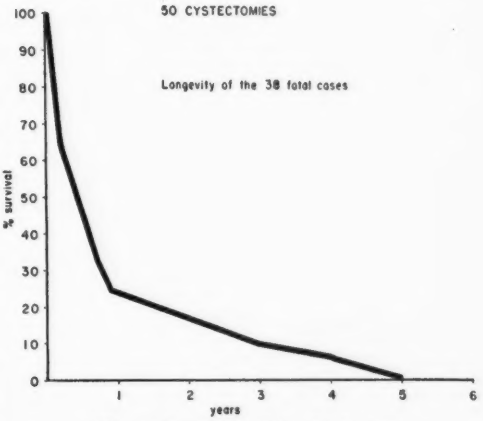

Fig. 1. Longevity of the fatal cases.

Although a few brilliant results have been obtained, the overall picture has been discouraging. The immediate postoperative mortality has not been high. The long term survivals have, however, been poor, the morbidity high, and the emotional depression and general misery of the patients have often been extreme. At first we inclined to ascribe this to our poor technique, but we eventually realized that these results were due to conditions which were beyond our control.

It must be recognized that in spite of brilliant developments in technique and after care the total operation of cystectomy is a formidable procedure for the patient. The surgeon frequently hesitates to recommend it

TABLE I.—LONG TERM SURVIVORS (4 TO 6 YEARS), 6 CASES

Case	Survival	Type implant	Preoperative upper tract	Rectal palpation	Cause of death
M.D.	Living 70 mos.	Cutaneous	Left hydronephrosis	Soft	
C. S.	Died 48 mos.	Cutaneous	Negative	Soft	Metastases
W. H.	Died 58 mos.	Coffey 1	Negative	Soft	Metastases
J. R.	Living 61 mos.	Cutaneous	Right nephrectomy for pyonephrosis	Soft	
W. G.	Living 63 mos.	Coffey 1	Left hydronephrosis	Soft	
R. W.	Living 55 mos.	Cutaneous	Right nephrectomy for papillary ca.	Soft	

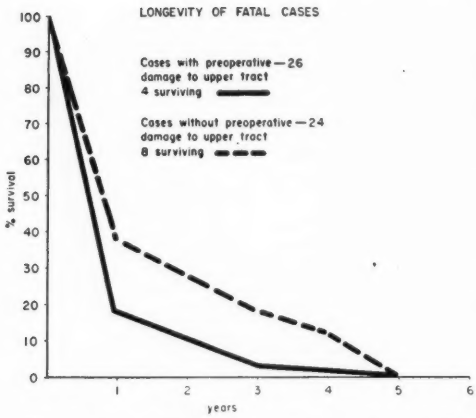

Fig. 2. Comparative longevity of cases with and without preoperative damage to the upper urinary tract.

and the patient refuses to submit to the operation until the tumor has grown out of hand and is beyond control by more conservative means. It is then too late to expect a long term survival and a possible cure. Unless the bladder is soft on rectal palpation and it practically falls out at operation it is too late for radical surgery. All of our 6 long term survivors (4 to 6 years) had soft bladders which came out easily. Even so, 2 have since died of metastases (at 48 and 58 months) and a third now has clinical evidence of metastases (at 61 months).

TECHNIQUE OF OPERATION

The technique of the operation is not difficult and can readily be mastered by any competent operator. The bladder may be removed by a suprapubic, retrograde retropubic, or combined abdominoperineal approach. We came to prefer the combined abdominoperineal method because it was more surgical and permitted better hemostasis. Node dissection is not a particulary difficult procedure. If the dissection is started at the pelvic brim and the iliac vessels are stripped, long vascular pedicles are developed for relatively easy ligation.

The total operation, including the transplantation of the ureters may be done in 1, 2, or 3 stages. Multiple stage operations, while reducing the immediate danger of uremia, have the great disadvantage of increasing the incidence of wound disruption, postoperative adhesions, and intestinal obstruction. The hospitalization also tends to be prolonged. We have found the 1 stage procedure, while carrying a greater immediate gamble, to be preferable.

Previous transurethral resections, coagulations, cystostomy, and radiation in various forms, render the bladder adherent, so that it is often torn open with a spill of its contents and tumor implantation into the bladder bed. In such cases it is too late for cystectomy.

PALLIATIVE CYSTECTOMY

Early in our series we removed a bladder for uncontrollable hemorrhage and bladder spasm 1 year after urinary diversion in an apparently inoperable case. The patient made a remarkable recovery and lived for 2 years, during which he carried on an active insurance business. This encouraged us to do a series of palliative cystectomies in obviously inoperable cases. Practically all of these patients did badly. The postoperative morbidity and misery for their short period of survival was extreme. Simple diversion of the urine without removal of the bladder seems to be preferable in such cases.

EARLY OPERATION AND THE HAZARDS OF URINARY DIVERSION

It is, therefore, obvious that from the standpoint of obtaining a radical cure of the carcinoma the bladder must be removed very early. The great stumbling block here is the diversion of the urine. It is our opinion that ureterosigmoidostomy, at least in its present form, is an unphysiologic procedure which carries with it a high ultimate mortality. The implantation of the clean ureter into the dirty, bacteria-laden bowel results in inevitable, ultimate pyelonephritis in a high percentage of cases regardless of the skill of the operator or the technique employed. All arguments on this point are futile. There is only one final answer, namely, objective 5 to 10 year statistics upon cases in which such operations are performed.

The risk of failure of such an implant is great if the ureter is dilated or the upper tract is infected. Ligating a dilated ureter, espe-

cially if infection is already present, is hazardous and is often followed by severe morbidity or mortality from pyelonephritis, pyonephrosis, or perinephric abscess, and the ensuing sepsis.

The ureterocutaneous implant is far safer. It is, however, messy, difficult to take care of, and not devoid of complications. These include decubitus from the indwelling catheter with resulting stricture, pyelonephritis, calculus formation, and periureteral abscess. Where no catheter is employed stricture of the ostium may cause trouble.

PYELONEPHRITIS AS A CAUSE OF MORBIDITY AND MORTALITY

Pyelonephritis, especially following ureterosigmoidostomy, is the great killer in cystectomy. In the tunnel techniques the hazard of upper tract stasis is present, and with the mucosa-to-mucosa techniques reflux is not uncommon. Chronic pyelonephritis may develop insidiously with a patent ostium and no evidence of stasis or dilatation of the upper tract on urography. Electrolyte imbalance is common. An appreciable rise in blood nitrogen values may only appear later. The patient may fail to show a comeback after surgery. His appetite is poor. He is listless and he gradually goes downhill. Such individuals may remain as hospital patients for many weeks or months until they finally die in uremia. In still other instances, after a brilliant recovery, with good urograms, normal blood chemistries, and a very satisfactory clinical convalescence, the patient returns to his home. After repeated satisfactory follow-up studies he suddenly experiences a collapse and returns to the hospital in a stuporous condition to die a short time later of uremia. Autopsy then reveals bilateral pyelonephritis. In 10 of the 14 of our patients who came to autopsy pyelonephritis was demonstrated and was a major or a contributing cause of the fatality.

In spite of these pitfalls a few hardy souls go on to a long term and comfortable survival. It is these fortunate individuals who spur on the ardent cystectomist to continued heroic efforts. The great majority of the patients, however, do badly. An analysis of the longevity reveals very few 5 year survivals. The greatest mortality is in the first year.

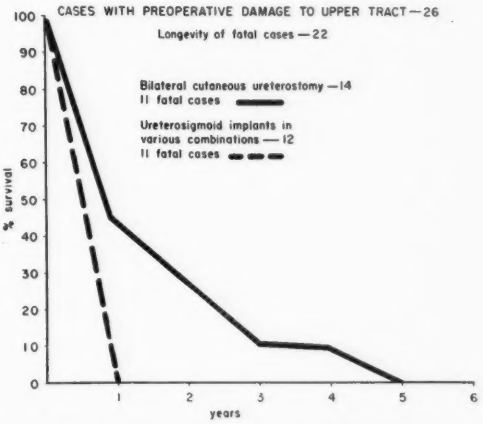

Fig. 3. Comparative longevity after cutaneous ureterostomy and ureterosigmoidostomy.

COMPARISON OF RADICAL AND CONSERVATIVE SURGERY

In comparison with these disastrous results the survival of patients treated by the commonly employed, more conservative measures is of interest. From 1932 to 1943, 567 cases of carcinoma of the urinary bladder were so treated at the Hines Hospital. The 5 year survivals were 27.6 per cent and the 5 year cures 20.9 per cent. The total hospitalization of the average patient was minimal as compared with that of the patient subjected to cystectomy, and the comfort of the survival in general far greater.

The high incidence of metastases in the cystectomy patient who comes to autopsy (5 of 14 cases in our series) reveals that many of these individuals come to radical surgery far too late to expect a cure of their carcinoma. To subject the patient with early carcinoma of the bladder to total cystectomy, however, seems to us unjustified because he will survive far longer and in far greater comfort if treated by more conservative means. The difference in this survival rate, especially during the first 3 years, is overwhelming. In view of these findings it seems to us that extensive node dissections will do little to improve the

survival and cure rate until a satisfactory and safe method for diversion of the urine can be devised.

SUMMARY

1. The operation of total cystectomy is a trying ordeal for the patient which is often accompanied by severe morbidity and a prolonged convalescence.

2. Although the immediate mortality is not high the long term survival rate is low. Very few patients live 5 years or more.

3. Chronic pyelonephritis resulting from ureterosigmoidostomy is the most important cause of ultimate mortality. This may occur regardless of the skill of the operator or the technique employed.

4. Cutaneous ureterostomy is safer, but it is messy, difficult to take care of, and not devoid of complications.

5. The removal of the urinary bladder offers a prospect of cure only if it is done very early in the course of the disease. But performed at this stage the accompanying diversion of the urine carries with it such a high morbidity and ultimate mortality that the patient will survive far longer and in far greater comfort if he is treated by more conservative means.

6. Until a safer and more satisfactory method of diversion of the urine is devised, expanding the scope of the operation will do little if anything to improve the long term survival rates.

7. Cystectomy is not justified as a palliative procedure in advanced carcinoma of the urinary bladder.

8. The indications for total cystectomy should, therefore, be placed with great caution and reserved for those cases in which no other form of treatment offers a prospect of relief.

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THE SURGICAL SIGNIFICANCE AND MANAGEMENT OF PATHOLOGIC BLOOD CLOTTING

GERALD H. PRATT, M.D., F.A.C.S., New York, New York

SURGICAL success or failure, and even life itself, often depends upon a knowledge of the cause and pathogenesis of abnormal clotting as well as prophylactic and corrective therapy of the condition. Pathologic venous clotting complicates up to 2 per cent of operative or obstetric procedures, and in special types of surgery (malignancy), it may affect 10 per cent of the patients. One must be humble in his approach to this subject. Our knowledge and experience has taught us much but there are many unknown links in the chain which changes liquid blood to clot. Surgical success has been dependent on the control of a quartet of killers: hemorrhage, shock, infection, and embolism. With blood replacement, modern anesthesiology, advanced surgical technique, and the antibiotic drugs, the first three of these killers, bleeding, shock, and infection, are more subject to our regulation. The fourth, thrombosis and embolism, remains a problem. All surgeons have experienced the sickening sensation of having a patient, often ready to be discharged as cured, die of an embolus. The hopelessness of this problem is realized as one tries to explain the occurrence to the family. Perhaps we have accepted this complication too complacently, and too often, as unpreventable. In the past year at Saint Vincent's Hospital in New York City, out of 4,917 operations, 176, or 3.5 per cent, postoperative deaths occurred. Eliminating the neurosurgical service with its invariable high rate (head wounds) of 25 per cent, we have a corrected mortality of 2.8 per cent. Eight per cent of these deaths were from thromboembolism. At Saint Clare's Hospital during the same period there were 4,700 operations and the mortality, uncorrected for neurosurgical deaths, was 6.8 per cent. The proved deaths from pulmonary emboli were 3 per cent of these. It is known that without autopsy many such deaths are designated as cardiac failures, myocardial insufficiency, and so forth so that the actual incidence is higher.

As surgeons, we are vitally concerned with the normal functioning of the clotting mechanism. Without it, operations would be impossible. Thus, man throughout his entire existence is almost constantly hemorrhaging and thrombosing. Normally, a perfectly balanced mechanism prevents either the tendency to bleed or to clot from becoming overactive. It is not surprising that it gets out of order sometimes.

The observations and suggestions presented in this article are based on a 20 year study in this field and upon a close study of over 10,000 general and vascular surgical operations. In addition, a detailed review has been made upon an average of 5 patients with pathologic venous clotting per hospital day for 7 years, a total of over 14,000 patient hospital days. Specifically, we have studied the effect of antibiotics, anticoagulants, blood transfusions, and surgical operations on the blood count, the platelets, the bleeding and prothrombin time, the protein fractions, and the amount of calcium in the blood. In discussing this subject in 1949 (8), it was mentioned that according to the *Cumulative Index*, there were 200 articles written each year on this subject. In 1951 there were over 650 articles written on this subject. It is obvious that if so many articles must be written, there is not only great interest in the subject, but the final answer to the clotting question is far from clear. The surgeon cannot accept a death rate of 1 or 2 out of every 1,000 operations from a pathologic clot without efforts to prevent such complications. We believe that this unconquered killer can be controlled.

From the Cardiovascular Clinic, Saint Vincent's Hospital and the New York University, Bellevue Medical Center, College of Medicine.

BLOOD CLOTTING MECHANISM

Biochemical factors. If we knew why blood remains fluid, we would be closer to the answer to our problem of pathologic clots. Under certain abnormal states such as jaundice, anemia, liver disease, and avitaminosis, bleeding tendencies increase. Some humans, such as hemophiliacs, inherit a tendency to bleed. Congenital clotters also exist in the same manner as bleeders are present in the population. The familial and environmental status play a part. In other diseases such as polycythemia and cancer, there is an increased clotting tendency. This may occur physiologically, also, as with obesity, increased cholesterol intake, and the changes following venous stasis. We cannot ligate all of the veins of the body between the operative site and the lung to prevent an embolism. Even if we did, it would be ineffective since most killer clots originate at other than the operative area (that is, the leg). This problem increases in importance as we operate upon older patients with diseases which have previously been considered incurable, as for example, cancer.

The early work of Morowitz and Howell brought out the "classical theory" of blood clotting. According to this theory, four substances were essential in order to cause clot: thromboplastin, calcium, prothrombin, and fibrin.

Old Theory of Blood Clotting

Thromboplastin + Prothrombin: Antiprothrombin $\longrightarrow$ Prothrombin

Prothrombin + Calcium = Thrombin

Thrombin + Fibrinogen $\longrightarrow$ Fibrin network

Fibrin + Erythrocytes: Leucocytes: Platelets = Blood clot

In the early 1940's, Quick found that five factors were necessary for a clot to form. Prothrombin actually consists of two substances. One of these is prothrombin which may arise from vitamin K since it decreases when there is a vitamin K depletion in the body. The other prothrombin factor was called, factor A or labile factor, by Quick, factor V by Owren, and Ac-globulin by Seegers. The body is rarely deficient in the latter factor.

Modern Biochemical Clotting Theories

$$\text{Thromboplastin} + \underset{\text{(both factors)}}{\text{Prothrombin}} \xrightarrow{C\,A\,++} \text{Thrombin}$$

$$\text{(Plasma Ac-globulin} \xrightarrow{\text{Thrombin}} \text{Serum Ac-globulin)}$$

$$\text{Prothrombin} + \text{Thromboplastin, if } \frac{C\,A\,++}{\text{Serum Ac-globulin}} \text{ are present, } \longrightarrow \text{Thrombin}$$

$$\text{Fibrinogen} \xrightarrow{+\text{Thrombin}} \text{Fibrin (clot)}$$

The action of thromboplastin is still unknown. It originates and becomes active when a platelet factor acts with a plasma constituent called a thromboplastinogen by Quick.

Quick's Formula for Blood Clotting

Thromboplastin complex (thromboplastinogen + platelet factor)

+

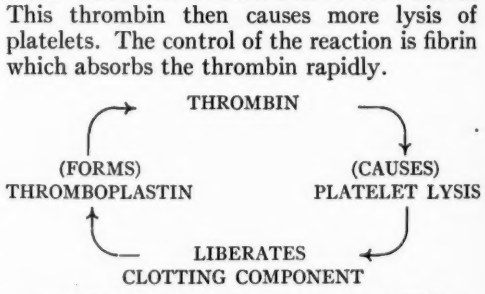
Prothrombin complex (Prothrombin radical + Calcium + Labile factor also called factor V or Ac-globulin)

$\downarrow$

THROMBIN + Fibrin $\longrightarrow$ Clot

A chain reaction appears to guide the five clotting agents, but a decrease in any one of the constituents may cause bleeding.

For the lysis of platelets, thrombin is required; as these cells liberate their clotting components, more thromboplastin is formed which causes more thrombin to be formed. This thrombin then causes more lysis of platelets. The control of the reaction is fibrin which absorbs the thrombin rapidly.



Fibrin clot controls reaction by absorbing thrombin.

Calcium is necessary for clotting but can be discounted as the necessary amount always exists in the body except in the presence of tetany. Thrombin activates fibrinogen. The

final fibrin is formed by the conversion of fibrinogen. The deeper one delves into the chemical theory of clotting, the more complex becomes the problem. "Clotting is a function of a number of variables" (1). Thus a perusal of what is known biologically and chemically of clotting leaves many blanks to be filled.

Physical-chemical factors. The physical-chemical side of the clotting problem is most important. Blood will remain in a fluid state for a long time if it is undisturbed and its container is intact. Thus an isolated blood vessel does not clot for some time if its endothelial lining is in continuity.

Physical factors favoring blood clotting.—We know that blood clots more rapidly: (1) if it is at body temperature, (2) if certain biologic substances, that is, certain poisons such as snake venoms are added, (3) if the blood is on a foreign surface, or (4) if the tissues containing it are injured or agitated.

Physical factors delaying clotting.—Delay occurs: (1) when an undamaged endothelial surface of the blood vessel is present, (2) if the temperature is lower, or (3) if the blood container is coated with paraffin or colloidin; (4) the addition of certain salts, such as sodium chloride, will reduce the clotting tendency, and (5) tissue extracts such as heparin, will keep the blood in a fluid state for an indefinite time.

The physics of clot.—The fibrinogen molecules and other blood components normally are prevented from adhesion to each other and to the blood vessel wall by a physical force. The electrical charge of both the blood constituents and their container is important and varies. Substances with the same electric charge are repulsive to each other. The red and white blood cells normally tend to repel each other. The positive ions are attracted to the wall. The zeta potential is the difference between the wall potential and the center of the solution which is considered to be zero. (The zeta potential is measured by producing a streaming potential as when blood is poured through a tube.) Heparin and other anticoagulants increase the negative charge or zeta potential. The blood flow is laminated. The blood cells are in the center of the stream surrounded by layers of plasma. The central cells move the most rapidly. Since the platelets are the smallest and the lightest components, they are on the outside. The platelets do not adhere to a normal intact wall, but when the wall is injured they immediately adhere to the site due to fibrin. Leucocytes become attached and the red cells join the mass with a resultant propagation of the clot.

Not only do the numbers of platelets increase to between two to three times normal postoperatively and postpartum, but they become more "sticky." The adhesiveness varies in different individuals at various times and under certain physiologic and disease states. Clotting occurs in certain patients after a "break" from not smoking, and this indicates that nicotine affects the adhesiveness of the platelets or cells, or both. In small vessels, occlusion can be produced by platelets alone and begins within 10 seconds after an injury with hemostasis occurring in 4 minutes. Anticoagulants reduce this adhesiveness. The rate of blood flow decrease in the capillary bed is minimal. An injury, therefore, affects the sludging more rapidly at the capillary level. With stasis, trauma, or certain disease states, such as malaria, the cells slow down on the lower side of the vessel. They may settle out when they reach a critical speed, as masses. Such settling will occur more rapidly in injured vessels or when the amount of fibrin is increased with a lowered electric charge. The reverse also is true in that if the repulsive electrical charges increase as with anticoagulant factors in the blood, there will be less clotting and less propagation of clot. The part that hydrophilic colloids play is uncertain but they are raised quantitatively after an operation and reduce the charge of the cells. Again, as in biochemistry, only the surface of the physical chemical possibilities of blood clotting have been lifted for our inspection.

To apply these factors surgically, it is apparent that any change in the relative cellular and fluid content of the blood can effect thrombosis. Thus, both an actual increase in the cells (polycythemia) or a relative elevation (hemorrhage) are stimulators of clot for-

mation. Hyperglobulinemia and hyperproteinemia cause more clotting. Age, obesity, as well as disease states, affect clotting. The postoperative starvation, blood loss, depletion of enteric content by enemas, diarrhea, or enterostomy, alter the physiology, and, if stasis is added, we have the factors for pathologic venous clotting. We emerge from discussion with three basic physical and biochemical points necessary for thrombosis; a fourth one is included. In order of importance from the surgical standpoint these are: (1) Change in the clotting tendency. From our previous discussion, it is apparent that we cannot label correctly or distinctly this component. This is our unknown. It probably controls itself if trauma and stasis are minimal. (2) Injury to the endothelial lining of the blood vessel. Injury is inevitable in a surgical or obstetric operation. Pressure on walls of the vessel occur during bed rest alone and this can disrupt the endothelium and instigate clot. Only a slight break in the continuity of the lining cells is necessary to initiate the clot formation. (3) Slowing of the blood stream. A reduction in the rate of blood flow at some points is usual with a surgical procedure. Anesthesia, depressing drugs, long periods in one position on the operating table, and bed rest, contribute to the stasis. Hemostats, ligation, and retraction are added causes. These two factors, trauma and stasis, are interrelated, as to cause and effect. Either one may result in the other. (4) Inheritance. A fourth factor must be included, and that is the thrombotic inheritance in certain families or individuals.

EFFECT OF OPERATION OR PATHOLOGIC CLOTS ON LABORATORY TESTS

In a 6 months' test, patients were divided into two groups, those undergoing general surgical procedures and those who were being treated for active thrombosis. Blood counts, bleeding times, sedimentation rate, the component proteins, the prothrombin time, and the platelet count were performed the day before the operation and on the first, third, and seventh postoperative days. The same tests, also, were done before and after the institution of antibiotic or antithrombotic therapy. While it is difficult to draw conclusions from any such study certain points or patterns emerged: (1) A surgical operation does not affect materially the hemoglobin or blood cell components or their differential count except if there is hemorrhage, blood replacement, or infection. (2) The bleeding and coagulation time is lowered slightly on the first to third day after operation, but returns to normal within a week. (3) The prothrombin time is decreased with operation and is increased with blood transfusion consistently, but only slightly unless the operation is excessively long or the amounts of blood transfused large. (4) There is no detectable change in the albumin-globulin ratio or the total protein content. (5) The platelets consistently double in number the day after operation but are back to normal within 7 days. The changes in their agglutinability have been noted. (6) The antibiotic drugs reduce the leucocyte count and the prothrombin time but do not effect other chemical changes. (7) The injectable antithrombotic drugs prolong bleeding time and affect the prothrombin time but little. The reverse is true with oral drugs. The effect in general is quantitative but varies with age, weight, and disease states. Heparin retardation, protamine heparin titration range, and other tests have been reported to be within so-called normal limits.

PREDISPOSING STATES IN WHICH ABNORMAL CLOTTING MAY BE EXPECTED

1. Cardiovascular disease (rheumatic heart disease-auricular fibrillation). Patients in this group terminate fatally from thromboembolic episodes in 1 out of 3 instances. In our 100 patients with fatal pulmonary embolism, 50 per cent had antecedent cardiovascular disease. In commissurotomy (8) operations for mitral stenosis, clots are found in the auricula in 20 per cent. Bailey reported this condition in 25 per cent.

2. Malignant disease. The co-occurrence of pathologic clotting and malignancy is established. Trousseau mentioned the coexistence of the two diseases 100 years ago. In 1 year we found 5 cases of cancer of the uterus in patients referred for an evident lesion in

the veins of the legs. The frequency with which phlebitis complicates carcinoma of the pancreas is established. The cause for the thrombosis is a release of thrombotic fractions with tissue destruction. The anticoagulant drugs are not as effective in the presence of carcinoma. Other degenerating diseases may cause clotting.

3. Age. More clotting occurs in the older patient. Ninety-five of our 100 patients with fatal embolisms were over 45 years of age.

4. Operation or delivery.

5. Obesity. The obese patient has an increased clotting potentiality. This can be demonstrated by administering a high cream diet in the experimental animal. There are twice as many postoperative thrombotic incidences in patients who weigh 200 pounds or over than in those under that critical weight. Gofman states that the large fat molecule may be the cause.

6. Fungus and allied infections. Fungus infection is present in most patients who have clotting episodes. Such infections may break the skin to permit the ingress of other organisms, or this complication may arise only in patients with diseased blood vessels.

7. Smoking probably precipitates clots.

PREVIOUS THROMBOTIC EPISODES AND PATHOLOGIC VARICOSE VEINS

Cold has a specific and predictable effect on blood. This is not the effect of temperature change alone as cold proteins can be precipitated. These produce agglutinins. The critical temperature of cold and clotting is approximately 37 degrees. The reduction of the body temperature to this level occurs normally only in the extremities. If the part is not warmed or is subjected to trauma, at the same time, severe arterial and venous clotting or destruction of tissue results.

The adrenal replacement or stimulating substance such as cortisone or ACTH cause increased thrombotic tendencies. Cosgriff and associates reported 7 per cent thrombosis.

The antibiotics sterilize the flora in the intestinal tract. Vitamin K is synthesized as the result of the bacterial action of the organisms normally present in the bowel. Lack of vitamin K increases the clotting tendency.

An undernourished physical status produces a defective coagulating mechanism. Overuse of alcohol has a similar effect.

TREATMENT

Small doses of antithrombotic drugs can be administered safely to the aged, the immobilized, those requiring large amounts of blood and antibiotics, and those with a previous history of venous trouble.

Active therapy. The therapy can be either surgical, medical, or both. The operative intervention places a physical obstruction between the source of the blood clots and the pulmonary artery. It has a place in therapy. The patients wisely selected for such intervention will have their lives saved. The other method is antithrombotic therapy.

The term anticoagulant drugs utilized for the past 10 years has become synonymous with hemorrhage to many surgeons. We propose that these drugs be called antithrombotic to denote the therapeutic application rather than to describe the occasional accident which follows their misapplication.

These antithrombotic drugs prevent propagation of clot and may possibly dissolve some clots. Correctly utilized these drugs eliminate the necessity of surgical intervention in many patients. There can be no inflexible or definitive type of therapy. The treatment depends upon the stage and extent of the disease and the response to therapy. The surgeon who decries all antithrombotic therapy, probably is unskilled in its use, and to cover such ignorance, cries "wolf." Equally dangerous is the internist who knows that there is a soft clot present in the femoral or iliac vein but refuses to suggest that the clot be blocked from the heart or lung by surgical ligation. Either of these extremes will result in deaths which we believe are preventable. When these drugs were introduced the fresh, surgical wound was placed first on the list of contraindications to their use. This forced the surgeon to use operative measures. The failure of such a one-sided program has been reported. Over 1,600 ligations on postoperative patients in one hospital in a year resulted in many vascular cripples. If the surgeon will individualize the patient, know the drug and

its action, and have a dependable laboratory, antithrombotic therapy in most surgical patients is safe and often life-saving. We have proved that such a program works in our clinic and believe that it will work in any other if the same care is exercised.

Operative intervention is indicated under some circumstances: (1) Postoperative patients who develop a pulmonary embolism or who have respiratory complications unexplained by physical or roentgenologic studies may require a ligation. These patients have a "soft," "silent," "bland," "undiagnosed" thrombus which may be an embolus between the first and fourteenth day. They do not have the inflamed, tender, febrile phlebitis. This latter group rarely have emboli because inflammation causes clot adhesion. If embolism does occur in this latter group it is usually small, late, and nonfatal. The latter group is not operated upon unless embolism occurs. (2) Ligation is performed for the patients in whom antithrombotic therapy is contraindicated, that is, a bleeding duodenal ulcer, a pulmonary tuberculosis, a cerebral, or chest wound. To these are added the few patients who do respond to the drugs. (3) If the symptoms indicate that the clot has propagated to the femoral or iliac veins, ligation is required. These individuals have the following symptoms: cyanosis, pain in the groin, abdomen, or back; mild edema; sense of fear; sentinel veins or an embolus (9). They may have signs in both legs. In these patients, clots are already present that are of sufficient size to block the pulmonary artery and cause death if they become emboli. Their lodgement in the lung, should they pass the pulmonary artery, would probably be fatal. The therapy in such instances is to place a mechanical block between this clot and the heart and lung.

The use of antithrombotic drugs in surgery is indicated in patients: (1) with inflammatory type of clotting, (2) not covered by indications for ligation, (3) after vascular surgery (blood vessel anastomosis), (4) with thrombosis seen or diagnosed late (i.e., 10 to 20 days), (5) after ligation for thrombosis.

All therapeutic measures require care in their application. We have been through the stage of anesthesia failure, danger, and even death, because the mode of its application was turned over to ill-trained interns or nurses who saw the patient for the first time when they placed a mask over their face. Digitalis or even aspirin can kill if an overdose is used. The laboratory reports must be reliable. The same is true of many chemical tests, and one cannot guide a diabetic or nephritic through a crisis with inaccurate laboratory data, or treat malignant disease if the pathology report is not dependable. A hemorrhage during antithrombotic therapy ordered by those well versed in its use should cast suspicion on the laboratory.

There are two main forms of antithrombotic drugs available for clinical use today: injectable substances, typified by heparin and an injectable coumarin drug which has recently been developed; and oral antithrombotic drugs.

Heparin quickly changes the coagulation time of blood. It has a strong negative charge and its action depends upon the inactivation of thrombin. It also acts as an antiprothrombin and may restrict platelet agglutination. Heparin complement is necessary for its action and it has a transitory action—10 milligrams lasting 40 minutes, 25 milligrams, 120 minutes, and 50 milligrams only 180 minutes. In our hands the subcutaneous injection of heparin is most satisfactory. From 30 to 70 milligrams every 3 hours maintains the coagulation time and the therapeutic level in most patients. The coagulation time (Lee-White method) should be checked before the administration of more drug. We have used heparin in massive doses of 200 milligrams given deep in the subcutaneous tissues of the leg by means of a fine needle. A definite pattern of response follows with a rise in the coagulation time to as high as 70 minutes in 4 hours and then a gradual subsidence with a continued therapeutic effect for 24 hours. In 25 patients so treated there was no bleeding. Intravenous heparin is used only after vascular operations. Injectable coumarin (1 mgm. per kgm.) has been given.

There are two main groups of oral antithrombotic drugs: the coumarin (dicumarol, tromexan, and cyclocumarol) and the in-

danedione (phenylindanedione). In general, dicumarol is maintained by a dose of 50 to 150 milligrams daily, tromexan 450 to 900 milligrams daily, and phenylindanedione by 400 to 600 milligrams daily. The dosage must be individualized, however, in each instance.

The use of antithrombotic drugs is contraindicated in the presence of: liver disease or jaundiced patients, advanced kidney disease, blood dyscrasias, pulmonary tuberculosis, vitamin K deficiency, vitamin C deficiency, gastrointestinal bleeding (peptic ulcer), certain fresh wounds (of the brain, lung, or if hemostasis is poor), late pregnancy, subacute bacterial endocarditis.

Hemorrhage due to antithrombotic drugs is best treated by its prevention. Overdose is dangerous. In the early days of anesthesia many patients died. An overdose of spinal anesthesia or pentothal will kill as quickly as a revolver. The failure to relieve a pneumothorax is as fatal as potassium cyanide. Yet, we do not hesitate to use anesthesias, to open pleuras, or even to put our hands and instruments within the human heart. In a similar manner, diligence makes these drugs safe.

The treatment of hemorrhage from the injectable drugs consists of: (1) stopping the drug; (2) application of local pressure and ice bags; (3) continuation of whole fresh blood transfusions; (4) intramuscular administration of protamine sulfate (50 mgm. in 5 c.c. aqueous solution every 6 hours; in severe hemorrhage 150 mgm. in 1 hour); (5) use of toluidine blue, a vasal dye, to counteract the heparin action (2 mgm. per kgm. of body weight is given intravenously).

The treatment of hemorrhage due to the oral thombotic drugs consists of: (1) discontinuing the drug; (2) local hemostasis; (It is wise to increase the pressure at the operative site) (3) whole fresh blood transfusions to supply prothrombin; (In from 2 to 6 hours this is used up and the prothrombin time rises again. The treatments must be continuous and continued until the bleeding has stopped both clinically and chemically.) (4) vitamin K active compounds. Vitamin K_1 is superior to vitamin K. Vitamin K_1 is supplied in an emulsion for intravenous injection as a 5 per cent solution. It acts in 15 minutes and reverses the prothrombin time range in 4 to 12 hours (usually 3 to 6 hours). The vitamin K substance must be continued and be combined with fresh whole blood. These drugs will stop the hemorrhage. Most accidents have occurred because of giving insufficient doses, not continuing them long enough, and not using the blood in combination.

For the treatment of inflammatory phlebitis we have used antithrombotic drugs in combination with sympathetic nerve blocks. In over 2,100 such blocks, there has not been a single hemorrhage.

In our clinic antithrombotic drugs have been used not sporadically but regularly and not for months but for years in the treatment of surgical patients. We have taken all the precautions necessary for safety, and in our hands the drugs have been safe. It is our contention that if these drugs can be used in one surgical clinic where all the safeguards necessary are taken they can be used in any clinic which has been similarly equipped provided the same safety measures are instituted.

SUMMARY

1. Some of the problems of blood coagulation in normal and pathologic states have been discussed.

2. With our present laboratory methods, the many unknowns make it impossible to select those patients in whom abnormal clotting will occur.

3. Physiologic and pathologic states which make clotting and bleeding more likely are known, and attention to each one of these will reduce the incidence of pathologic clotting.

4. The rejection of antithrombotic drugs for surgical use is untenable. These drugs can be administered with safety if their action is known, if the laboratory analysis is correct, and if due care is exercised. Indications for operative intervention exist but are limited.

5. New drugs or fractions of old drugs will be developed which will be safer.

6. Hemorrhage from these drugs is preventable. If it does occur it must be treated actively and continuously.

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STUDIES OF HEMODYNAMIC CHANGES IN HUMANS FOLLOWING INDUCTION OF SPINAL ANESTHESIA

IV. Observations in Low Spinal Anesthesia During Surgery

SALVATORE M. SANCETTA, M.D., R. B. LYNN, M.D., F.R.C.S., F. A. SIMEONE, M.D., F.A.C.S., GLADYS HECKMAN, R.N., and HANNA JANOUSKOVEC, R.N., Cleveland, Ohio

THE OBSERVATIONS made in a series of 6 consecutive unselected patients operated upon under low spinal anesthesia are reported herein, and the following additional features are commented upon: (1) the dangers of inadequate anesthetic levels in the waking surgical patient; (2) severe hypotension of unknown etiology, as differentiated from simple spinal anesthetic hypotension; (3) the use of vasopressor drugs; (4) the unknown cause of spinal anesthetic bradycardia.

The general hemodynamic changes following high spinal anesthesia, with and without operation, and those following low spinal anesthesia in patients not undergoing surgery have been described in previous reports from this laboratory (4, 5). In these reports low spinal anesthesia was arbitrarily defined as "that which blocks conduction as high as the fourth thoracic segment, but not higher, and, in contrast to high spinal anesthesia, causes vasoconstriction in the upper extremities." In the present study, the anesthetic level varied from the eleventh to the seventh thoracic levels.

MATERIAL AND METHODS

Six patients, ranging in age from 23 to 66 years and free of cardiopulmonic disease, were operated upon for various surgical indications. Following bedtime administration of 0.1 gram of phenobarbital and an overnight fast, the patients were given a morning dose of pentobarbital sodium (0.1 gm.) and transported to an air-conditioned laboratory where the temperature was maintained at between 23 and 24 degrees C.

Cardiac catheterization was performed under fluoroscopic control and continuous electrocardiographic observation. Pressure readings were obtained in the right atrium and in the pulmonary artery, and basal cardiac outputs and finger blood flows were recorded. The tip of the catheter (No. 7F) was left just within the right pulmonary artery, and the catheter taped to the forearm. The patients were then given preoperative morphine and atropine (0.010 and 0.0004 gm. respectively, doses which cause no significant hemodynamic alterations) and taken to the operating room. Intrathecal procaine or pontocaine was administered by barbotage to produce an anesthetic level between the eleventh and seventh thoracic segment. Surgery was then initiated, and cardiac outputs, pressure, and peripheral flow determinations were made 30 and 60 minutes following administration of the anesthetic. All studies were done with the patients supine (no tilt); *supplemental anesthetics and vasopressor drugs were not employed at any time.*

Brachial arterial pressures were obtained through an indwelling No. 19 intra-arterial needle, transduced via Statham strain gauges and recorded on the Brush multichannel oscillograph. Right atrial or pulmonary arterial pressures were simultaneously inscribed. Mean pressures were derived by planimetric integration of the pulse contours in two successive respiratory cycles. Peripheral flows were measured by placing an oncometer on the second digit of the arm not used for catheterization and intra-arterial puncture and by employing air transmission, Grass and Statham strain gauge transduction, and Grass oscillographic plethysmographic recording (6).

From the Departments of Medicine and Surgery of Western Reserve University School of Medicine at City Hospital, Cleveland, Ohio.

This investigation was supported by a grant (No. H-1382) from the National Heart Institute of the U. S. Public Health Service.

TABLE I.—THE HEMODYNAMIC AND BLOOD OXYGEN CHANGES INDUCED BY LOW SPINAL ANESTHESIA (MEAN PRESSURES ARE IN PARENTHESES)

Patient		L.H	R.T.	R.W.	D.B.	L.G.	E.C.	Averages	Percentile change
Age and sex		59 F	66 F	47 M	23 F	41 M	44 M	46.7 —	— —
Operation		Imp. radium (Ca. cervix)	Exc. ulcer, graft (leg)	Bil. saphenous stripping	Exc. ulcer graft (leg)	Revision leg stump	Amputation of toe	— —	— —
Anesthetic and level, mgm.		Th 7 Procaine 100	Th 11 Pontocaine 12	Th 11 Pontocaine 12	Th 8 Pontocaine 12	Th 11 Pontocaine 22	Th 11 Procaine 100	— —	— —
Brachial arterial pressure (mm. Hg)	Control	126/78 (99.9)	138/78 (109.0)	120/72 (92.8)	119/86 (103.0)	123/84 (102.0)	126/70 (96.0)	— (100.5)	— —
	30 min.	82/55 (66.0)	114/54 (82.0)	63/39 (50.0)	54/39 (45.7)	115/79 (91.0)	87/59 (72.5)	(67.9)	−32.4
	60 min.	75/49 (58.0)	120/60 (88.0)	69/45 (53.8)	72/54 (62.0)	99/78 (86.0)	— —	(69.6)	−30.7
Right atrial pressure (mm. Hg)	Control	6.0/2.1 (4.0)	4.5/2.2 (3.3)	7.2/1.6 (5.6)	6.4/2.6 (4.2)	— (3.2)	5.1/1.5 (3.2)	(3.9)	—
	60 min.	2.0/—1.0 (1.1)	4.2/1.8 (2.8)	4.3/1.2 (3.1)	3.2/1.0 (2.2)	— (3.2)	—	(2.5)	−34.6
Pulmonary arterial pressure (mm. Hg)	Control	23.5/11 (16.6)	25.7/8.0 (14.0)	28.5/8.0 (13.9)	22.7/7.0 (12.5)	22.0/10 (15.5)	26.5/9.0 (15.0)	(14.1)	—
	30 min.	16.0/7.0 (11.4)	22.4/7.0 (12.1)	22.0/6.0 (10.9)	17.2/6.1 (9.1)	21.7/10 (15.4)	22.0/6.0 (14.2)	(11.9)	−15.6
	60 min.	15.6/7.1 (11.3)	23.0/7.0 (12.3)	25.0/7.0 (12.5)	17.0/6.0 (9.3)	22.0/10.0 (15.4)	— —	(11.8)	−16.3
Finger blood flow (c.c./10 c.c. part/min.)	Control	1.62	0.22	0.29	1.13	0.60	0.81	0.78	—
	30 min.	1.13	0.33	0.24	1.02	0.50	1.03	0.71	−9.0
	60 min.	1.18	0.44	0.22	0.16	1.80	—	0.76	−2.6
Cardiac output (c.c./min.)	Control	4780	5436	6638	4870	5400	5423	5424	—
	30 min.	3660	3059	5741	3575	5440	5072	4423	−18.4
	60 min.	3200	3493	6254	3391	5740	—	4416	−18.4
Stroke volume (c.c./stroke)	Control	62.0	65.5	90.0	57.3	63.6	57.0	66.0	—
	30 min.	40.2	34.7	76.0	47.0	39.5	50.0	48.0	−27.3
	60 min.	42.2	42.0	83.0	40.8	49.8	—	51.6	−21.8
Pulse rate (/min.)	Control	77	83	73	85	85	95	83	—
	30 min.	91	88	75	76	136	101	94	+13.8
	60 min.	76	84	75	83	115	—	86	+4.2
Oxygen consumption (c.c./min.)	Control	194	193	235	189	229	250	215	—
	30 min.	172	145	240	143	249	246	199	−7.4
	60 min.	157	169	239	135	324	—	205	−2.8
Oxygen capacity (Vol. per cent)	Control	14.85	12.55	16.55	15.42	17.25	17.85	15.74	—
	30 min.	15.23	12.35	16.00	14.06	17.46	17.53	15.44	−1.9
	60 min.	14.85	12.35	15.64	14.06	17.25	—	14.83	−5.8
Brachial art. O_2 content (Vol. per cent)	Control	13.92	11.39	14.89	14.52	16.38	16.48	14.60	—
	30 min.	14.10	11.46	14.63	12.60	16.54	15.81	14.20	−2.7
	60 min.	13.70	11.29	14.26	12.96	16.08	—	13.66	−6.4
Pulm. art O_2 content (Vol. per cent)	Control	9.86	7.84	11.35	10.64	12.14	11.88	10.62	—
	30 min.	9.39	6.72	10.45	8.60	11.96	10.96	9.68	−8.8
	60 min.	8.79	6.44	10.44	8.98	10.54	—	9.04	−13.9
A-V oxygen difference (Vol. per cent)	Control	4.06	3.55	3.54	3.88	4.24	4.61	3.98	—
	30 min.	4.71	4.74	4.18	4.00	4.58	4.85	4.51	+11.7
	60 min.	4.91	4.85	3.82	3.98	5.54	—	4.62	+13.8
Arterial O_2 saturation (Per cent)	Control	93.7	90.7	90.0	94.1	94.9	92.3	92.6	—
	30 min.	92.6	92.8	91.5	89.6	94.7	90.2	91.9	−0.7
	60 min.	92.2	91.4	91.2	92.1	92.6	—	91.9	−0.7

All determinations on specimens for blood oxygen content were performed in duplicate on the Beckman DU spectrophotometer (2). Samples of inspired and expired air were analyzed for oxygen on the Pauling oxygen analyzer and corrected for STP in the final computation of oxygen consumption and cardiac output. Left ventricular work (LVW) and estimated total peripheral resistance (ETPR) were calculated according to standard formulae.

RESULTS AND DISCUSSION

The data relevant to these cases are presented in Tables I and II. The cardiac output and index, stroke volume, oxygen consumption, brachial, right atrial, and pulmonary arterial pressures generally decrease. Arteriovenous oxygen differences show no significant alterations, but directional changes point uniformly to an increase. Arterial oxygen saturation is essentially unaltered, though occasionally it shows a slight decrease. Brachial arterial oxygen content undergoes variable changes, but more often than not is decreased, these changes being reflected in the oxygen capacity. The causes for this decrease have not been fully assessed (hematocrit levels show similar trends), although the peripheral trapping of red cells is probably partly responsible. Generally the decrease shows a correlation with the height of the anesthetic and the decrease of the cardiac output, at times this decrease being quite marked (D.B., Table I). This is an important consideration in anemic patients.

In 3 of the 6 patients the finger blood flow was increased, rather than decreased, in the operating room as compared to the basal values, due to the fact that at the time the operating rooms were not air conditioned, the temperature being sometimes as high as 32 degrees C. LVW and ETPR are reduced, the former a desirable feature from the standpoint of cardiac efficiency and related changes in the coronary blood flow.

The results and changes mentioned are quite similar to those noted in patients who were given spinal anesthesia and who were investigated entirely in the laboratory (5), hence not faced with the anxiety induced by the expectation of surgery. The only demonstration of this latter feature was the tendency for the pulse rate to increase, with a consequently accentuated decrease in the stroke volume, whereas in patients not undergoing surgery the pulse rate, after an initial and transient increase during and immediately after the administration of the anesthetic, usually returns rapidly to the basal level or actually decreases. Even so, in the present series (L.G., Table I) only 1 patient showed a marked increase in the heart rate. The surprising absences of differences due to anxiety and the surgical procedure are testimony to the steady state that may be achieved by the use of patients emotionally suitable for study —by proper conditioning, clinical handling, and anesthetic and surgical technique. The fact that no intra-abdominal surgery was performed (except in A.R., *vide infra*) may account for the greater variability in the results obtained by Sven Johnson in a similar study performed on 13 surgical patients (all of whom had intra-abdominal procedures) although the overall directional changes were similar to those noted in our group; 8 of his patients showed a marked tachycardia. The use of the customary dose of ephedrine (0.050 gm.) may have been an added factor in his series.

DANGERS OF INADEQUATE ANESTHESIA

Unintended changes observed in a young woman emphasize the necessity of insuring that spinal anesthesia, when employed in the waking patient, be adequate.

CASE 1. A.R., female aged 24 years. The diagnosis was acute pelvic inflammatory disease with pyometrium. The operative procedure consisted of total hysterectomy, salpingo-oophorectomy through a low abdominal midline incision. The anesthetic used was pontocaine by barbotage, 0.015 gram, to a level of the seventh thoracic segment.

The initial incision was made 15 minutes after the administration of the anesthetic. Exploration of the upper abdominal compartment with the gloved hand resulted in an immediate and continued complaint of pain and great anxiety. At this point surgical interference was stopped for 10 minutes and hemodynamic observations made. Following these, supplemental gas-oxygen-ether anesthesia was instituted and the study discontinued.

Table III illustrates the changes, most of which, though expected, would not be noted

TABLE II.—THE CARDIAC INDICES, LEFT VENTRICULAR WORK AND TOTAL PERIPHERAL RESISTANCE

Patient		L.H.	R.T.	R.W.	D.B.	L.G.	E.C.*	Averages	Percentile change
Cardiac index (Lit./sq.m./min.)	Control	2.86	3.33	3.28	3.00	3.00	—	3.09	—
	30 min.	2.19	1.88	2.85	2.20	3.00	—	2.42	−21.3
	60 min.	1.91	2.15	3.09	2.09	3.18	—	2.48	−19.7
Left ventricular work (Kg.M./minute)	Control	6.46	8.00	8.32	6.77	7.44	7.01	7.33	—
	30 min.	3.26	3.38	3.87	2.20	6.68	4.96	4.06	−44.5
	60 min.	2.50	4.14	4.53	2.84	6.67	—	4.14	−42.1
Total peripheral resistance (Absolute units)	Control	27.8	26.7	18.7	28.4	24.9	23.6	25.0	—
	30 min.	24.0	35.8	11.6	17.0	22.4	19.2	21.7	−13.2
	60 min.	24.2	33.7	11.5	24.4	20.0	—	22.7	−9.9

*Index not calculable (old amputation, left leg).

and probably not appreciated clinically. Particularly outstanding are the marked increase in the heart rate, the great increase in cardiac output, which almost doubled, and a serious decrease in the oxygen saturation from 93.1 to 84 per cent. It is reasonable to attribute these changes to the effects of pain and to diaphragmatic stimulation with consequent decrease in tidal volume. Anxiety may have been responsible in part for the tachycardia. There was no significantly increased motor activity of the unanesthetized motor regions—a fact which is borne out by the decreased oxygen consumption. An older patient might not have tolerated this experience as well.

Severe hypotension which occasionally follows simple spinal anesthetic hypotension; the use of vasopressor drugs. Progressively higher levels of spinal anesthesia are associated with progressively greater decreases in the brachial arterial pressure and in the cardiac output (5). The evidence favors the view that the variant degree of spinal sympathetic blockade is responsible for these changes. The resultant hypotension may be termed "simple spinal anesthetic hypotension." Even when marked, though gradual decreases in blood pressure occur (such as in patients R.W. and D.B., Table I), these decreases are not unexpected and not surprising. They are of no consequence provided a steady blood pressure plateau is maintained, and it would not appear wise at this stage to administer a vasopressor, which can mask the slowly developing and insidious decrease in blood pressure which may occur later and that somehow appears related to gradual blood loss and visceral manipulation. A vasopressor administered at this stage ought to be considered an emergency measure, to be followed by fluid replacement therapy to increase an already decreased effective circulating blood volume. In "simple spinal anesthetic hypotension" the initial blood pressure and cardiac output decreases average between 15 and 30 per cent for low spinal anesthesia, as against high spinal anesthesia where, depending on the situation, reductions of as much as 70 per cent have been observed (4). In both instances the difference is one of degree, with the exception of the vasoconstriction noted in the digits of the hand when the anesthetic level is below the fourth thoracic segment (at constant ambient temperatures). The skin is warm and pink, peripheral flow is well maintained, and oxygen saturation remains unaltered, especially when cautious barbotage is employed. In the absence of psychic or appreciable emotional stimuli, the heart rate is only slightly and transiently increased. The rate of blood flow is decreased in the splanchnic and coronary beds, unaltered in the cerebral bed of normotensive subjects, but probably adequate in the absence of vascular disease of the organs involved, since no lasting damage may be demonstrated by the ordinary tests employed. Finally, such a decentralized vascular bed is very responsive to small doses of parenterally administered vasopressor drugs, and the blood pressure may be elevated rapidly at will.

There is no evidence that such an elevation is necessary or even desirable; if use of such drugs is thought to be essential—and this actually is a moot point—norepinephrine, which is least likely to produce an increase in the heart rate, would theoretically appear to be the drug of choice. It may be noted in passing that maintenance of a preanesthetic level of blood pressure by concomitantly administered vasopressors is no guarantee against damage to selective organs as a result of the anesthesia. In a carefully controlled study conducted by Dr. Henry Beecher and his group (1), in which low spinal anesthesia was administered to patients without infection for surgical procedures not involving handling of the liver or nearby organs, 5 of 10 patients with normal preoperative bromsulphalein retention tests developed postoperative abnormalities, despite the prophylactic administration of ephedrine to prevent hypotension.[1] The causes for these alterations are not clear, and it cannot be stated with certainty that an oxygen debt (associated with a decreased splanchnic flow) may not be selectively incurred, despite failure to demonstrate the former.

Such "denervation" type of hypotension must be differentiated from what, for want of a better term, may be called "severe hypotension of unknown cause," not due to hemorrhage or visceral manipulation. This usually occurs suddenly and dramatically, some time after the anesthetic level and blood pressure appear to have become stabilized (usually 10 and 25 minutes respectively), although it may occur precipitously from the moment the anesthetic is administered. It is more often noted in the aged and in individuals with large vessel sclerosis and systolic hypertension. Whether prophylactic administration of a vasopressor will prevent this is not certain; certainly it occurs in spite of such medication. The skin is cold and may become livid; brachial arterial blood shows no significant decrease in oxygen saturation, yet cyanosis of the mucous membranes and nail beds (stagnant anoxia) may be present. If decrease in blood pressure is significantly critical, plethysmographic observation reveals a decrease in blood flow in the digits of both hands and feet, and administration of vasopressor drugs does not produce the dramatic increase in blood pressure which is noted in "simple spinal anesthetic hypotension." This is truly severe hypotension of unknown causation, not immediately responsive to any single measure but requiring the utmost in immediate correction, transfusion being the one single most effective measure. An illustrative case follows.

[1]Beecher, H.K. Personal communication.

TABLE III.—DATA IN PATIENT A.R. (DESIGNATIONS AS IN TABLE I)

	Basal values	30 min. post-anesthesia
Heart rate	72	117
Pulmonary arterial pressure	19.5/8.0 (14.1)	17.0/8.4 (13.0)
Brachial arterial pressure	111/59 (77.4)	70/47 (55.4)
Pulmonary arterial O_2 content	12.13	11.84
Brachial arterial O_2 content	15.56	13.87
Arteriovenous difference	3.43	2.03
Oxygen capacity	16.70	16.50
Oxygen saturation (arterial)	93.1	84.0
Oxygen consumption	170	163
Cardiac output	4956	8029
Cardiac index	3.04	4.92
Stroke volume	68.8	68.6
Peripheral flow (finger)	0.13	0.064

CASE 2. M.S., male aged 66 years. Clinical working diagnosis was: (1) unknown disease of gastrointestinal tract; (2) medial arteriosclerosis (moderate); (3) systolic hypertension (170/110, clinical); (4) pulmonary emphysema, slight. Precatheterization sedation consisted of pentobarbital sodium 0.1 gram at bed time and repeated in the morning.

This patient was selected for the study of low spinal anesthesia in the absence of surgical intervention, and observations made in the catheterization laboratory. After the basal studies, 100 milligrams of procaine were administered by barbotage and within 15 minutes the anesthetic level was fixed at the seventh thoracic segment. The blood pressure appeared stabilized at 130/60 twenty-five minutes after the anesthesia, but as preparations were being made for the 30 minute observations, the patient suddenly began to hyperventilate and complain of nausea, although he did not retch. None of the peripheral pulses could be felt and intra-arterial blood pressure was recorded as 28/26. The skin turned livid and gray, and even with maximal amplification of the plethysmographic apparatus, peripheral flow and volume in the digits of all extremities could not be registered. Brachial arterial oxygen saturation, previously 91 per cent, was virtually unaltered (89.1 per cent). Ventilation was not grossly impaired and the patient remained conscious throughout. Treatment consisted in transfusion with 500 cubic centimeters of whole blood (initiated

within 25 minutes of the onset of the episode), 15 degrees' head Trendelenberg tilt, repeated small doses of intravenous neosynephrine, and administration of 100 per cent oxygen. No noticeable improvement was noted until after transfusion was begun. Gradually he improved and, about 90 minutes after the onset of this crisis, had recovered. Brachial arterial pressure was now 160/90 and oxygen saturation 93 per cent. Throughout this episode, ST 1, 2, 3 showed definite sagging and TV 4, 5, 6 became flat, definite evidence of subendocardial ischemia. The electrocardiogram returned to the precatheterization normal within 4 days.

Because of concern for the patient, cardiac outputs, central pressures, and arterial and mixed venous blood samples for oxygen content were not studied.

SPINAL ANESTHETIC BRADYCARDIA

The heart rate does not undergo marked change as a result of low spinal anesthesia alone. In high spinal anesthesia a relative bradycardia usually, although not always, ensues. This has been attributed either to paralysis of the cardiac accelerator nerves or to a reverse Bainbridge reflex. If this is true, it is puzzling to find cases in which low spinal anesthesia has been given, and in which in spite of a marked decrease in systemic arterial pressure (R.W. & D.B., Table I) the hydrostatic carotid sinus reflex has failed to produce the expected tachycardia. This is an interesting problem and merits further investigation.

SUMMARY

1. The general hemodynamic changes consequent to low spinal anesthesia in waking patients undergoing surgery are presented. Vasopressor drugs were not employed in this investigation.

2. Data illustrating the dangers of inadequate anesthetic levels are presented.

3. An attempt is made to differentiate between simple spinal anesthetic hypotension and severe hypotension which is of unknown cause.

4. The role of vasopressor drugs is briefly discussed.

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TREATMENT OF INGUINAL HERNIA IN INFANCY AND CHILDHOOD

GEORGE B. PACKARD, M.D., F.A.C.S., and CARL H. McLAUTHLIN, M.D.,
Denver, Colorado

HERNIA is so common at all ages that its potential danger is not generally appreciated. The United States mortality figures for 1948, according to Elman, show hernia responsible for 5,000 deaths, a higher figure than that of appendicitis. The mortality figure for hernia has remained at the same level for two decades while that for appendicitis has been cut to one-third. As fatalities in hernia are due mainly to strangulation or obstruction, the problem would seem best solved by preventive herniotomy.

The commonest hernia is the indirect inguinal, a congenital defect frequently found in infancy and childhood, an age when repair is relatively simple and usually lastingly effective. Naturally parents are fearful of operations on their babies and struggle with trusses and reductions in the hope that the child may "outgrow" his hernia. But in the large majority, the hernia remains or reappears at a later date. Physicians are partially responsible for the presence of so many hernias, as many practitioners are reluctant to advise operation at an early age.

I want to present our experience at the Denver Children's Hospital with the surgical treatment of hernia in infants and children covering our last 681 consecutive cases. Three hundred forty-nine of these were reviewed by Dr. H. Calvin Fisher and cover the years 1945 to 1950; the other 332 operated on during the past 3 years are summarized by my associate, Dr. C. H. McLauthlin and myself. Analysis of this fairly large number suggests some conclusions that may be worth consideration. There were 602 males and 79 females, about 8 males to 1 female. There were 451 hernias on the right, 163 on the left, and 67 bilateral—nearly three times as many hernias on the right as on the left side.

From the Department of Surgery, Denver Children's Hospital.

We believe that indication for surgical repair exists whenever the diagnosis of hernia is made, regardless of age. The only exception is a sickly child or an infant that is not gaining weight. Hernia in infancy and childhood is due to the persistence of a processus vaginalis which normally is closed at birth (Fig. 1). It is probable that an occasional patent processus may close spontaneously in the first year of life though it will not close unless kept constantly empty. It can be kept constantly empty only by the continuous application of a truss—which means all day and all night regardless of bath time, toilet time, or clothes changing. The prolapse of abdominal contents for a minute cancels the least gain. This is a tremendous job for parents; trusses are dirty and messy, they must be watched all the time, and even then slip out of place when least expected. Trusses may favor lack of normal muscle development. After a year of the best parental care, a few hernias may be cured, but most recur rather promptly while some reappear after a few months or years.

Without a truss, and even sometimes with one, the commonest and most serious complication of a hernia which has not been operated upon is incarceration or strangulation. The younger the child the greater the chance for incarceration. In this series, there were 72 patients sent into the hospital with irreducible hernias, an overall percentage of 10½. There were many others who had a history of incarceration. The great majority of these incarcerations were in the first year of life; 56 of them occurred among the 214 infants, 1 year old or under—an incidence of a little over 26 per cent.

In spite of the large number of incarcerations, strangulation to the extent of requiring resection was rare. The small intestine in the male is the commonest occupant of the hernia sac. In our series, only 2 intestinal

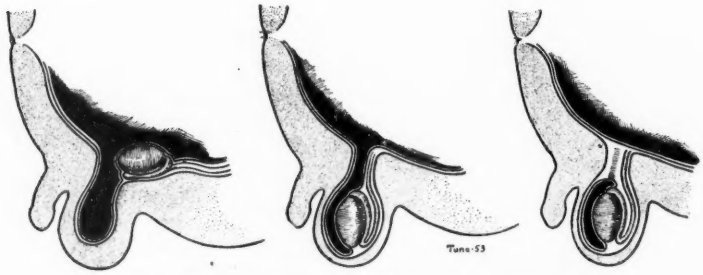

Fig. 1. Normal descent of testicle and closure of processus vaginalis.

resections were required. In one, 23 centimeters of gangrenous ileum were resected, in the other a Meckel's diverticulum with a small border of ileum was removed. In the female, a painful irreducible ovary is not uncommon. In the last 35 females, an ovary was found in the sac in 15. In 1 case, a gangrenous ovary required resection, a rare complication, reported elsewhere by Pender and associates. These 3 were the only resections in 681 cases. The rare need of resection in these many incarcerations is apparently due to the early pain which disturbs the parents and brings the baby to the physician promptly.

When a child, usually an infant, arrives at the hospital with an incarcerated hernia, the usual treatment is the following. If the incarceration has been present for longer than 12 hours or if there has been blood in the stool, immediate operation is done. Otherwise, reasonable, not forcible, attempt at reduction is made. If this is unsuccessful, the baby is given a sedative, usually seconal by rectum, and put in Trendelenburg position. In most of the cases, this accomplishes reduction. If the mass is still there after 2 hours, operation is promptly carried out. If reduction has been successful without surgery, operation is usually postponed for 3 to 4 days to allow edema and bruising to subside.

There was no direct hernia in these 681 cases. In fact no muscle weakness was noted, the hernia being due entirely to the patency of the processus vaginalis. Removal of this patent processus or hernia sac with the least possible injury to the neighboring tissues, if done without technical error, should give 100 per cent cure. The technique of the simple but adequate operation is not new. The procedure described by Turner in 1912 is very similar to the operation described in the more recent reports of Coles, Larsen, Potts, and Duckett.

The incision, 1 to 2 inches long, is transverse in the abdominal crease of babies and may be in the same location in older children. This incision leaves a better scar than does the oblique inguinal, is less likely to be followed by keloid, and is a little easier to keep from contamination. There is really no objection to the oblique inguinal incision as used in adults, however, and it may give a little better exposure if the operator is not accustomed to the transverse. The incision is carried down to the external oblique fascia, the external ring identified, and the fascia split (Fig. 2). Opening the external ring gives a little better exposure of the cord. The cremaster is opened rather widely to expose the cord and sac. The ilioinguinal nerve is displaced laterally. Without disturbing the cord in its bed, the surgeon meticulously dissects out the sac, and, after assuring himself it is empty, transfixes and ties it at the neck where the properitoneal fat appears. After the sac is amputated, a running suture is taken in the remaining cuff so that there may be no possibility that this tie will give way. Fine silk or cotton is the suture material preferred. This sac ligation is the crux of the operation. The secure closure of the neck should prevent any recurrence; great care must be taken to avoid tearing this very thin and fragile sac tissue. Any hydrocele of the cord is removed with the sac; a sac extending to surround the testicle or an attached hydrocele of the tunica vaginalis is

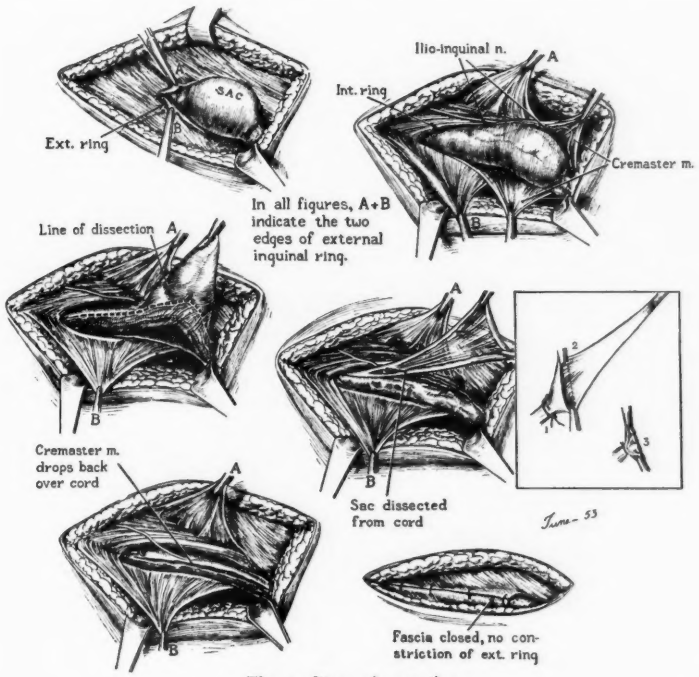
SAC
Ext. ring
Ilio-inguinal n.
Int. ring
Cremaster m.
In all figures, A+B indicate the two edges of external inguinal ring.
Line of dissection
Cremaster m. drops back over cord
Sac dissected from cord
Fascia closed, no constriction of ext. ring

Fig. 2. Steps of operation.

removed down to the testicle and the distal end left wide open. No eversion or bottle operation is done. That finishes the operation except to close the external oblique fascia and the skin. Any transplant of the cord is absolutely contraindicated; revision of the inguinal floor as approximation of the internal oblique to the inguinal ligament is unnecessary. There is no muscle weakness in this area; suture or displacement may even interfere with normal muscle development. The fascia is closed without the least constriction of the external ring. The skin may be closed as desired, subcuticular sutures of fine cotton or silk obviate the difficulty of later suture removal. Bilateral repair may be easily accomplished by extending the same skin incision.

At our hospital which has a large private staff, the operations were done by 48 surgeons some of whom could not resist a Ferguson type of repair. Even a few Bassinis were done. The majority follow the method described which is fast becoming the standard procedure.

In these 681 cases, there was 1 death, in a known hemophiliac with an irreducible mass. In spite of minimum surgery, preoperative and repeated fresh blood transfusions, the patient died from massive extraperitoneal hemorrhage.

There were in these 681 cases, 4 recurrent hernias which had been operated on at this hospital. One recurrence followed simple sac removal; the same surgeon at his second operation was sure that he had not satisfactorily obliterated the sac the first time. The other 3 recurrences included 1 Ferguson and 2 cord transplant repairs from which one gains the impression, at least, that additional inguinal floor support and cord transplant did not add to the effectiveness of the operation.

The recurrence rate while less than ⅔ of 1 per cent is higher than others recently reported. It is, however, very low in a hospital open to a large staff with some variance in skill, and is far lower than the incidence of trouble connected with expectant treatment.

Other postoperative complications have been few and remarkably mild. Nearly every young patient had a little elevation of temperature on the day following surgery. Wound infection was not a feature though occasionally a note was made regarding a reddened wound or a moist suture; there were no breakdowns. Bleeding from the operative wound, easily controlled, was reported twice.

Not too long ago, all of our infants and young children were restrained in bed for a full week. Our present plan, which is the rule in many other places, puts no restriction on infants at all; they wear diapers and usually go home the day after surgery. A minimal dressing of elastoplast is used and left in place until the patient returns for his first dressing at about 1 week. Older children are not confined to bed but an attempt is made to restrict their activities for about a week and not to send them to school until 2 weeks after operation. For a patient to go home the day after hernia surgery seems a little drastic to the cautious surgeon, but, after all, these hernia patients look better and have fewer complications to fear than the posttonsillectomy patients in whom early dismissal from the hospital has been the rule for years.

Of these 681 patients, 602 were males and 79 females; 104 of these males had hydroceles. Hydrocele in infancy or childhood is almost always associated with a hernia sac and represents a portion of the processus vaginalis that has not been obliterated. It is of interest that 3 of these patients were operated on by urologists for hydrocele who then had to complete a hernia repair. Hydrocele in the female was comparatively rare.

Undescended testicle is not uncommonly associated with inguinal hernia and is corrected at the time of hernia repair. Infancy is not our choice of time for this correction, but, in case of incarceration, the complete operation is done.

As it is much more difficult to detect a hernia that is not out in infants and young children than in adults, determination of possible hernia on the opposite side is most inaccurate. The appearance of a hernia on the opposite side after one repair is an annoyance to the surgeon and most distressing to the parents. Hernia in children is not diagnosed by inserting a finger in the ring and trying to get the patient to cough or strain—he will do just the opposite. Gentle palpation of the cord, if an empty sac is present, will reveal an undue thickness of the cord and sometimes a feel of rub. If there is such a suggestion on palpation or if an observant parent reports swelling on the opposite side, bilateral exploration should be done—it takes but little longer, a transverse incision can be easily extended, it saves later embarrassment—and it is surprising how often a second sac will be found.

In this series, 23 patients returned for hernia on the side opposite to the original repair. Fifteen of these had had a right repair and returned with a left. Eight had had a left repair and returned with a right. As right inguinal hernia was three times as common as the left in this series, as in others, it might be argued that left inguinal hernias are more likely to be followed by a right than vice versa, but the figures are not impressive enough to make bilateral repair a routine measure.

DISCUSSION AND CONCLUSIONS

As one goes over the records of these 681 cases, he is impressed by the fact that the surgical treatment is far better than the expectant and that operation is the treatment of choice whenever the diagnosis is made. The danger of incarceration and emergency care in the infant, the use of dirty trusses, the long continued anxiety of the parents are obviated by a short operation and a short hospital stay which is practically without risk.

The operation however must be meticulous. Delicate separation of the sac is mandatory to avoid any injury to the cord or tear of the sac before the secure transfixion suture is placed. Careful technique is the basic consideration in this operation as complete sac removal with secure neck ligation is the secret of success.

Recurrence is so rare that when it does occur, it suggests technical error. Apparently the simple removal of the sac is as effective as any other method. Some tightening of the ring in large hernias may possibly be indi-

cated, but it is hard to see how the approximation of the internal oblique to the inguinal ligament over the cord (Ferguson method) can be of any help; and transplantation of the cord by the Bassini type of repair seems absolutely contraindicated.

Success in the operation from this series or others reported would seem to have no relation to postoperative restraint or to length of hospital stay.

While recurrence on the same side is a remote possibility, every effort should be made to detect the presence of hernia on the opposite side in order to avoid a second operation.

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THE SYMPTOMATOLOGY AND MANAGEMENT OF PROSTATIC CALCULI

DAVID PRESMAN, M.D., Chicago, Illinois

IT HAS become evident in recent years that prostatic calculi occur much more frequently than had been previously realized. Although the pathogenesis and symptomatology of prostatic calculi were fully described by Thompson in 1861, the importance of this clinical entity has only become recognized in the past two decades. The relatively high incidence of prostatic calculi was strikingly demonstrated by the work of Randall. He analyzed a series of 324 routine autopsies on males and found 86 cases or a 26.5 per cent incidence of prostatic calculi. Further interest in this subject was stimulated by the excellent studies of Young, Thomas and Robert, Moore, Gutierrez, Kretschmer, Huggins and Baer, and others. Today, urologists are becoming more aware of the importance of diagnosing the presence of prostatic calculi in order adequately to evaluate the proper management of the patient with prostatic disease. It is purposed herein to review a series of 48 patients with prostatic calculi especially with regard to the symptomatology and management.

There are two general types of prostatic calculi: the endogenous or true calculi and the exogenous or false calculi. True prostatic calculi are much more common and develop within the substance of the prostate gland. Thompson postulated the theory that they are formed by deposition of calcium salts on the corpora amylacea. This belief is still held today by most urologists although specific proof is lacking. A comprehensive study by Moore demonstrated that the corpora amylacea are formed from desquamated epithelial cells and prostatic secretion. He concluded that the increased incidence of corpora amylacea in senility is the result of a variety of factors which act through increased epithelial desquamation and stagnation in the ductile system.

From the Department of Urology, Chicago Medical School, Michael Reese and Cook County Hospitals.

True prostatic calculi are almost always multiple and vary in size from millet-seed or smaller to pea-sized. The very small, almost microscopic, calculi are not visualized on x-ray and are often encountered during transurethral prostatic resection. This rather common experience emphasizes again the relatively high incidence of this condition. Prostatic calculi are dark brown in color and are usually irregular in shape, sometimes containing many definite facets. They are found within the substance of the prostate gland most commonly in the acini and ducts. Extrusion of the calculi into the stroma of the gland may occur. Complete block of the ducts by calculi may produce cystic dilatation of the corresponding acini with the formation of a pseudodiverticulum containing other calculi. In some instances the calculi are located near the opening of the ducts just beneath the mucosa of the prostatic urethra and may be seen cystoscopically. They are occasionally extruded into the lumen of the urethra and may be voided spontaneously or fall backward into the bladder to act as a nucleus for the formation of bladder calculi. These appear usually as multiple small, brownish calculi, cuboidal in shape, and lie in the bas-fond of the bladder. In the presence of benign prostatic hypertrophy, prostatic calculi are usually found posteriorly at the periphery between the adenoma and the false capsule. They may become imbedded in the substance of the false capsule so that they may be left behind in the prostatic bed after enucleation.

The chemical composition of prostatic calculi was studied by Huggins and Baer. They found that the principal inorganic constituent is tertiary calcium phosphate, presumably with an apatite constitution. Carbonate is somewhat less than in bone; otherwise chemical and x-ray analysis reveals close similarity of the inorganic constituents of prostatic calculi and the bone salt. The organic compon-

cents, about 20 per cent, include protein, cholesterol, and citrate.

False or exogenous prostatic calculi are relatively rare and differ basically from true calculi. False calculi form in the prostatic urethra and do not primarily involve the prostate gland. They may be derived from calculi originating in the upper urinary tract or from true prostatic calculi which have been extruded and become lodged in the prostatic urethra. They may also form within the prostatic bed following any type of prostatectomy and protrude into the bladder itself in the shape of a dumbbell which has given rise to the term "dumbbell calculus" in the older urologic literature. False prostatic calculi are usually single and with the constant deposition of calcium salts from the urine may reach a very large size; the so-called giant prostatic calculus. This usually produces some degree of bladder neck obstruction and, as a rule, requires surgical intervention.

ANALYSIS OF CASES

This series of cases comprises a total of 48 patients of which 46 had true prostatic calculi and 2 had false calculi. Each group will be considered separately since each presents different clinical problems. A brief case report will be given on the 2 patients with false calculi. The series of true prostatic calculi will be analyzed in detail in order to summarize the important aspects of the clinical picture and management. In each patient the diagnosis was made by a routine flat film of the abdomen. All but 3 cases were seen as private patients and have been followed carefully for from 6 months to as long as 15 years.

TRUE PROSTATIC CALCULI

Age incidence. Prostatic calculi occur predominantly in the middle and older age groups. There were 7 cases in the fifth decade, the remainder were patients above the age of 50. Twelve patients (26 per cent) were in the sixth decade, 16 (35 per cent) in the seventh decade, 7 (15 per cent) in the eighth decade, 4 (9 per cent) in the ninth decade. It is of interest to note that the incidence of 15 per cent in patients below the age of 50 is of some significance and should warrant a careful consideration of the possible diagnosis of prostatic calculi in the young adult with persistent prostatic symptoms.

Associated prostatic pathology. Associated prostatic pathology was present in 36 cases or 78 per cent. This includes chronic prostatitis 39 per cent, benign prostatic hypertrophy 39 per cent, 1 patient with prostatic carcinoma, and 20 per cent without other pathology.

The high incidence of associated prostatitis and hypertrophy is striking and is substantiated by similar findings as reported by Randall, Young, and Gutierrez. It is believed that the prostatitis develops secondarily to the calculi because of partial obstruction of the prostatic ducts with inadequate drainage of prostatic secretion and also secondary infection due to the presence of a foreign body. The relationship of benign hypertrophy and prostatic calculi is more difficult to explain. In these cases the calculi are almost always found outside the hypertrophied gland between the adenoma and the false capsule. It is possible that compression of the prostatic ducts in the normal portion of the gland during the development of the hypertrophy leads to some degree of obstruction with subsequent stagnation of prostatic secretion and the formation of prostatic calculi. At any rate the common association of chronic prostatitis or benign prostatic hypertrophy with prostatic calculi is an established clinical fact and should be kept in mind when evaluating the clinical management of these patients.

There was 1 case of coexistent prostatic carcinoma and calculi. Cristol and Emmett reported a series of patients who had undergone transurethral prostatic resection. They found true prostatic calculi in 6 per cent of malignant lesions of the prostate. While this is not very high, it may nevertheless be significant and the coexistence of these two lesions should always be kept in mind lest a carcinoma of the prostate be overlooked. The differential diagnosis on rectal examination may be very difficult, and, if indicated, further procedures should be performed in order to obtain a biopsy of the prostate.

There were 9 patients without demonstrable associated disease in the prostate. In most of these, prostatic calculi were diagnosed by x-ray

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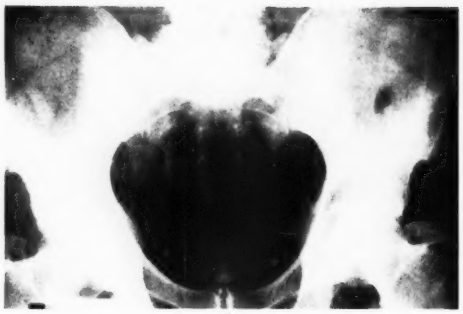

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Fig. 1. Plain films demonstrating prostatic calculi for which no therapy was given. a, Asymptomatic prostatic calculi; b, asymptomatic prostatic calculi; c, prostatic calculi causing one episode of mild transient symptoms which subsided spontaneously.

during the course of other studies. Two patients had transient mild perineal discomfort for which a flat film was taken and the diagnosis established. No therapy was prescribed for any of the patients in this group. There are unquestionably a large number of individuals who develop prostatic calculi which are never discovered because of lack of symptoms. It is probable that most of these patients will remain asymptomatic throughout their lifetime unless they develop an associated prostatitis or benign hypertrophy. The incidental finding of asymptomatic prostatic calculi is of no clinical significance and requires no further therapy.

Rectal examination. In only relatively few patients with prostatic calculi can the diagnosis be made by rectal examination since in most cases the calculi are too small to be palpated. Of this series of 46 cases there were 8 or 17 per cent which were diagnosed in this manner. A sensation of crepitation is rarely elicited and is felt only in the presence of large and very numerous prostatic calculi. In some instances a localized area of induration or irregularity is palpable which may be suggestive of prostatic calculi. As a rule this lacks the feeling of fixation that is felt with carcinoma of the prostate but occasionally the rectal findings may be equivocal. It is to be emphasized, therefore, that a definite diagnosis of prostatic calculi may only be made by the x-ray. A flat film of the prostatic region should be considered an essential part of the work-up of all patients with prostatic symptoms.

Symptomatology. The symptomatology of the patients in this series may be classified into three groups: those patients who were asymptomatic (17 per cent); those with mild symptoms (47 per cent); and those with moderate to severe symptoms (35 per cent). It will be seen that the number of patients who were

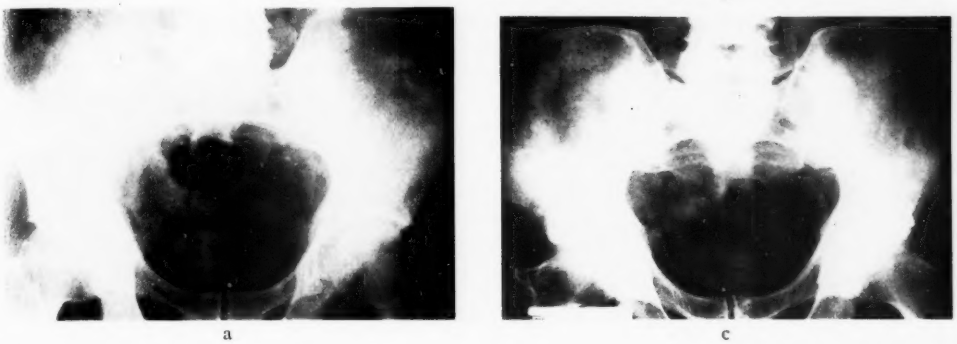

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Fig. 2. a, b, c, Plain films of 3 patients with prostatic calculi and associated prostatitis causing moderate symptoms. Satisfactory relief of symptoms obtained with periodic prostatic massage and administration of gantrisin.

symptomatic (82 per cent) approximates the incidence of associated prostatitis or benign hypertrophy (78 per cent). In other words, the presence of symptoms in patients with prostatic calculi is closely correlated with the incidence of associated disease in the prostate. This would seem to corroborate our clinical impression that the symptomatology of prostatic calculi in most cases is primarily due to the accompanying prostatitis or benign hypertrophy rather than to the calculi themselves.

The presenting complaints were variable, the most common (31 cases) being urinary in nature. Urinary dysfunction included frequency, dysuria, slowing of the stream, and nocturia. Other common symptoms were backache (10 cases), suprapubic or perineal discomfort (10 cases), pyuria (19 cases), and hematuria (9 cases). One patient was asymptomatic, except for several episodes of chills and fever which subsided with a course of antibiotics.

The relatively common occurrence of pyuria and hematuria was striking. In all of these patients, there was an associated chronic prostatitis or benign hypertrophy. Upper urinary tract studies were normal except for 2 cases which had small renal calculi. It is important to keep in mind that the finding of blood or pus in the urine may indicate the presence of prostatic calculi.

There were 3 patients with hemospermia supposedly due to an accompanying seminal vesiculitis. Although hemospermia was not a common symptom in this series, it may occur more frequently in the presence of prostatic calculi than is generally suspected. If routine roentgenograms were taken of all patients with hemospermia, the known incidence of prostatic calculi in this syndrome would probably be much higher.

It is apparent that the symptomatology in patients with prostatic calculi simulates the clinical picture seen with uncomplicated prostatic hypertrophy or chronic prostatitis. As a rule, there is nothing pathognomonic in the urologic history or findings in the patient with prostatic calculi definitely to establish this di-

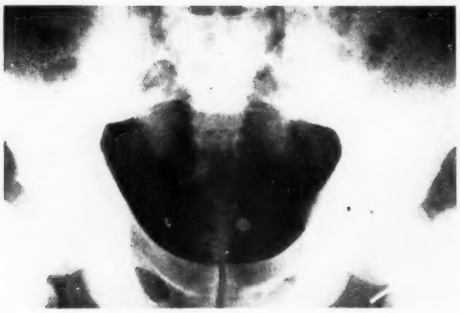

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Fig. 3. a, b, Plain films of 2 patients with extensive prostatic calculi and associated prostatitis causing recurrent gross pyuria and prostatic secretion loaded with pus. These patients have been practically asymptomatic for 8 and 15 years respectively, requiring only occasional prostatic massage.

agnosis. The symptomatology in most instances is a reflection of the associated hypertrophy or prostatitis. This emphasizes once more the importance of the routine flat film in patients with prostatic symptoms. Those patients with prostatic calculi but without associated pathology were usually either asymptomatic or had very mild transient complaints. It is only the infrequent case with very large and numerous prostatic calculi that the symptoms may be ascribed to the calculi per se.

Calculi in other portions of the urinary tract. There were 8 patients with calculous disease in either the bladder, ureters, or kidneys. It is known that bladder stones may form from extruded prostatic calculi which pass into the bladder and continue to enlarge by deposition of calcium salts from the urine. The significance of associated calculi in the upper urinary tract is not clear but may be due to some abnormality of calcium metabolism predisposing to the formation of stones anywhere in the genitourinary tract.

Management. Our experience has been that in most patients with prostatic calculi, therapy is indicated primarily for the associated disease in the prostate rather than for the prostatic calculi. The exception is the infrequent case with very large multiple calculi which requires surgical removal in order to effect symptomatic relief. Of the 46 patients in this series, there were 16 patients or 35 per cent who received no therapy of any kind; 20 patients or 43 per cent were treated with prostatic massage and medication; and 10 patients or 22 per cent had surgery performed. A total of 78 per cent of the patients, therefore, did not require any operative procedure. This demonstrates the fact that in the vast majority of individuals with prostatic calculi, conservative management is indicated.

The group in which no therapy was given comprises those patients who were either asymptomatic or who had mild transient symptoms which subsided spontaneously. It is possible that in some of these cases progressive symptoms may develop in the future so that additional therapy may be warranted. In all likelihood, however, the prostatic calculi will remain quiescent in most instances and cause no further difficulty (Fig. 1).

The group of patients who were treated with prostatic massage and medication were those with definite symptoms and an associated chronic prostatitis. In several the symptoms were probably due to a slight degree of prostatic hypertrophy which also responded well to the measures mentioned. Periodic prostatic massage and the administration of gantrisin or terramycin controlled the prostatitis very adequately with an excellent symptomatic result in all of these patients (Fig. 2). As a rule, both the urine and prostatic secretion became free of pus cells. The presence of prostatic calculi

a

b

c

Fig. 4. a, b, Plain films of 2 patients with prostatic calculi and associated prostatic hypertrophy for which transurethral resection was performed with removal of the prostatic calculi. An excellent functional result was obtained in both individuals. c, Removed calculi from case b.

may predispose to recurrent episodes of prostatitis at variable intervals in some of these patients. However, these recurrences should be managed by the same conservative measures and will usually respond very well to this regimen.

In a few instances, although the patient becomes asymptomatic and has no complaints, the urine and prostatic secretion continue to show pus. It is believed that in this type of patient with persistent or recurrent pyuria and pus in the prostatic secretion but without any symptoms, conservatism is still indicated. It is questionable whether more radical procedures such as surgical intervention would produce any more beneficial results. It is assumed, of course, that in these cases, a complete urologic study including an intravenous urogram and cystourethroscopy reveals no other pathology in the genitourinary tract. The theoretical danger of a long-standing low grade infection in the prostate secondary to prostatic calculi has proved in most cases to be without foundation. We have observed several such patients over a period of many years who have been quite healthy and have not developed any further difficulty or complications (Fig. 3). To submit these asymptomatic individuals to a major operative procedure in order to eliminate a small localized walled-off area of infection which is causing no trouble seems like a rather heroic measure which accomplishes little and might lead to more serious complications.

Surgical intervention is indicated for two general groups. First, those patients who have an associated prostatic hypertrophy of a sufficient degree to cause obstructive symptoms which would require surgery for relief of symptoms. The mere presence of prostatic hypertrophy and prostatic calculi is not an indication for surgery. Each case must be evaluated on the basis of degree of obstructive uropathy. The second group includes those cases with very large and numerous prostatic calculi which appear to be the primary cause of the symptoms.

The choice of operative approach depends upon several factors which necessitate careful evaluation of the individual patient. With an associated prostatic hypertrophy, the size of the gland should determine whether an enucle-

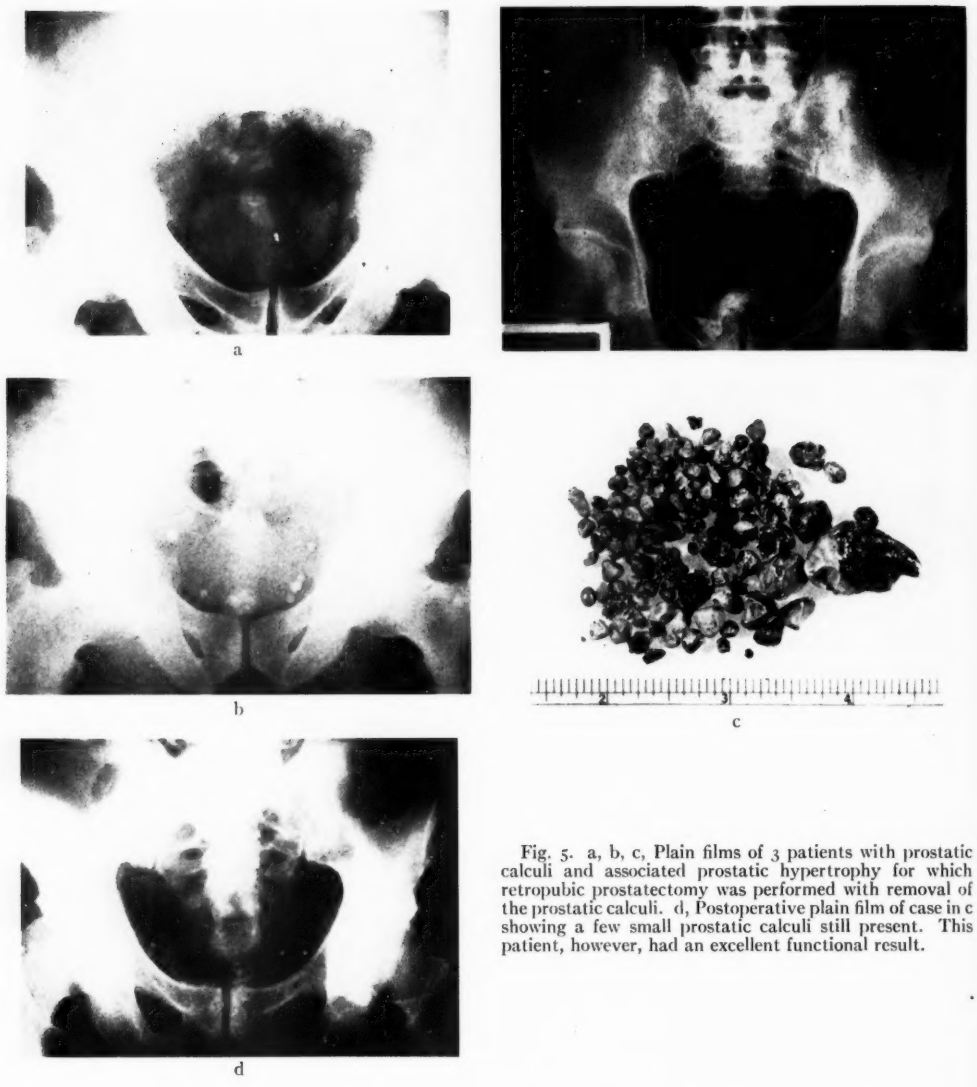
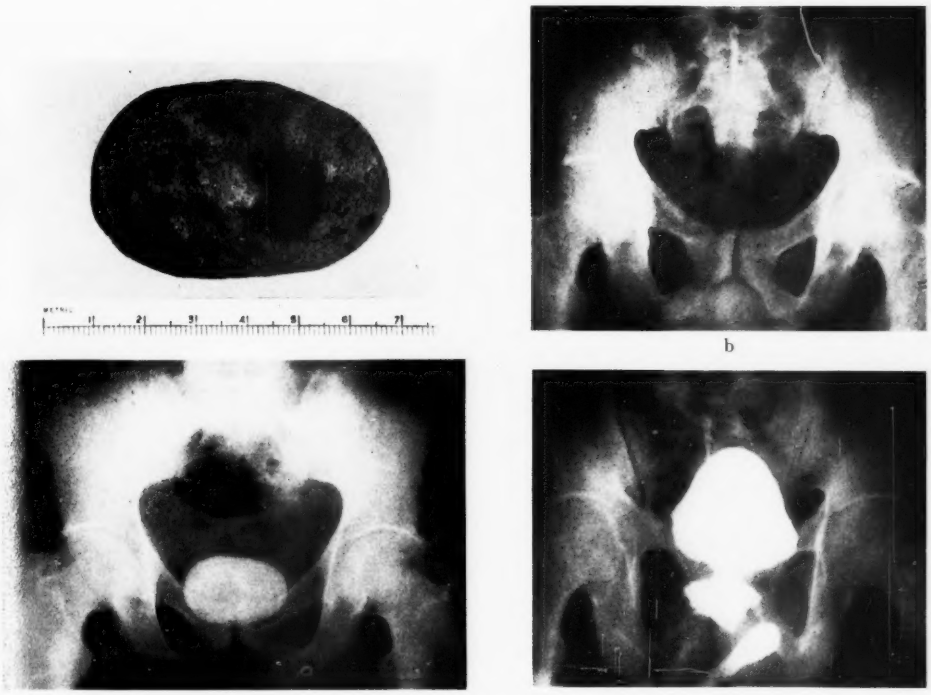


Fig. 5. a, b, c, Plain films of 3 patients with prostatic calculi and associated prostatic hypertrophy for which retropubic prostatectomy was performed with removal of the prostatic calculi. d, Postoperative plain film of case in c showing a few small prostatic calculi still present. This patient, however, had an excellent functional result.

ation or transurethral resection should be done. The latter procedure is best reserved for the smaller glands since the prostatic calculi lie between the adenoma and the false capsule. A complete resection must be performed down to the capsule in order to expose the calculi so that they may be dislodged and evacuated through the resectoscope sheath. If some of the calculi are too large, they can be pushed into the bladder and crushed with a lithotrite. We have had excellent results with this procedure in selected cases. Our experience is in accord with Emmett who reported that complete removal of all the calculi is not essential to a good functional result. If the obstructing prostate is completely resected



a b c

Fig. 6. X-ray film demonstrating giant false prostatic calculus which formed without previous prostatic surgery. a, Preoperative film and calculus which was removed perineally. b, Plain film, 1 year postoperative, no recurrence. c, Cystourethrogram 1 year postoperative showing wide bladder neck and dilated prostatic urethra.

and most of the calculi removed, a satisfactory result is usually obtained with a relatively conservative procedure. Of the 10 patients operated upon in this series, 5 had a transurethral resection performed with good results (Fig. 4).

In those patients with large prostates, open enucleation is to be preferred. In some instances the prostatic calculi may be so adherent to the posterior false capsule that partial excision of this structure may be necessary to remove the calculi adequately. This is probably best accomplished by either the retropubic or perineal approach. The suprapubic transvesical route is less satisfactory since the posterior capsule is not as accessible so that it may not be technically feasible to excise it if necessary.

Although perineal prostatectomy offers a direct approach by which the posterior capsule may be excised, this operation has certain disadvantages such as the high incidence of impotence and the occasional occurrence of postoperative incontinence and perineal fistulas. We have preferred the retropubic approach since the prostatic bed can be visualized directly after enucleation of the prostate and most of the calculi removed under direct vision. Excision of portions of the posterior capsule can also be performed when necessary without difficulty and without the danger of any troublesome postoperative complications. Our results in 5 patients who had retropubic prostatectomy and prostatolithotomy were uniformly good. In one patient with very large multiple calculi, a few calculi were left in the prostatic bed as shown by the postoperative roentgenograms; however, this procedure apparently did not affect the functional end result (Fig. 5).

Fig. 7. Plain film showing giant false prostatic calculus which formed in the prostatic bed several years after suprapubic prostatectomy.

FALSE PROSTATIC CALCULI

The 2 cases of false prostatic calculi in this series demonstrate several unusual features. A brief case report of each patient will be presented.

CASE 1. A 56 year old male was admitted to the hospital with a history of progressive urinary symptoms for the past 3 years. He complained of frequency, nocturia, difficulty in voiding, slowing of the stream, and perineal discomfort. The general physical examination was essentially negative. Rectal examination revealed a stony hard, smooth, symmetrical mass in the region of the prostate. Urinalysis showed a gross pyuria. The blood urea nitrogen, acid and alkaline phosphatase were within normal limits. Flat plate of the abdomen revealed a large ovoid calcific shadow over the bladder region with the characteristic appearance of a bladder calculus. Cystoscopy was performed under sodium pentothal anesthesia and a large calculus was seen which appeared to occupy a very small capacity bladder.

Ten days after admission a suprapubic cystotomy was performed for the purpose of removing the large bladder calculus. However, on opening the bladder, no stone could be seen or palpated. There was a hard smooth mass palpable under the trigone. The bladder neck was markedly contracted and would not admit the examining finger. It was then realized that the patient had a large prostatic calculus which was partially subtrigonal. Because of the contracted bladder neck and the size of the calculus, it was believed that any attempt to remove the stone transvesically would result in severe trauma to the bladder neck and trigone. Accordingly, the bladder was closed around a mushroom catheter.

One week later a perineal approach was made with the patient in the lithotomy position. After freeing the rectum, the posterior prostatic capsule was incised and the calculus was exposed. The capsule was separated from the calculus which was then removed without difficulty. The prostatic bed appeared as a large, smooth cavity at the proximal end of which a small contracted bladder neck could be palpated. The bladder neck was extremely fibrous and fixed and could not be brought down for adequate exposure. Because of this, it was decided to do a transurethral revision of the neck as a third stage procedure. An indwelling urethral catheter was inserted and the posterior prostatic capsule was closed. The postoperative course was uneventful.

Ten days later a transurethral revision of the bladder neck was performed and 3 grams of tissue were removed. Two weeks later the suprapubic fistula was healed and the patient was voiding well (Fig. 6).

CASE 2. A 68 year old male was admitted to the hospital because of urinary frequency, nocturia, and dysuria of 2 years' duration. Five years previously a suprapubic prostatectomy for benign prostatic hypertrophy had been performed. The general physical examination was essentially negative except for a healed midline suprapubic scar. Rectal examination revealed a large hard smooth mass in the region of the prostate. The urine showed a gross pyuria. Urea nitrogen, acid and alkaline phosphatase were normal. Flat plate of the abdomen revealed a large pear-shaped calculus within the prostatic bed.

A suprapubic cystotomy was performed 1 week after admission. The bladder appeared normal throughout. A large calculus could be palpated within the prostatic bed. The bladder neck was rather wide and after some manipulation the calculus was loosened from the prostatic bed, delivered into the bladder, and removed. It was partially broken during this procedure but all pieces were removed. The bladder was closed around a mushroom catheter.

The patient had an uneventful postoperative course and was discharged with a good functional result (Fig. 7).

These 2 cases illustrate several interesting features of false prostatic calculi. The first case is unusual in that a giant calculus formed within the prostate or prostatic urethra without the predisposing factor of previous surgery. The original nidus for the stone was probably a small prostatic calculus which became lodged within the prostatic urethra and by enlarging it gradually replaced the prostate gland. Because of the markedly contracted bladder neck, any attempt to remove the stone transvesically would have resulted in extensive injury to the neck and trigone. A perineal approach proved to be quite simple and the stone was easily removed without damage to soft tissue structures.

The second case is an example of the type of false prostatic calculi which form in the prostatic bed several years after a prostatectomy. Although in this patient the stone was limited to the prostatic bed, many of these stone project into the bladder in the form of a dumbbell and have been termed "dumbbell calculi." These occurred more commonly prior to the advent of the sulfonamides and antibiotics because of the frequent complication of postoperative infections which apparently predisposed to stone formation. They are rarely seen today since severe infection of the prostatic bed can be adequately prevented. The diagnosis is suggested by rectal palpation of a stony hard smooth mass in the region of the prostate and is confirmed by the x-ray picture. As a rule, a suprapubic transvesical approach is indicated for the removal of the stone and usually presents no particular difficulty.

False prostatic calculi are usually solitary and grow to a large size so that the term "giant prostatic calculus" has been applied. This is in contradistinction to true prostatic calculi which are always multiple and small. The symptomatology of false prostatic calculi is similar to that seen with any type of prostatism. There are no characteristic or distinctive symptoms. The diagnosis is made by x-ray examination. Management of these patients is necessarily surgical with removal of the calculus. This may be done in one or two stages with a preliminary cystotomy depending upon the general condition of the patient. The specific operative approach should be determined in each individual patient according to the size and site of the calculus.

SUMMARY AND CONCLUSIONS

1. A study of 48 patients with prostatic calculi is presented. This series comprises 46 patients with true prostatic calculi and 2 patients with false prostatic calculi.

2. True prostatic calculi occur predominantly in individuals above the age of 50 although 15 per cent of the patients in this series were in the fifth decade.

3. Associated prostatic disease is frequent. Either chronic prostatitis or benign prostatic hypertrophy was present in 78 per cent of the patients with true prostatic calculi. Coexistent carcinoma and calculi occurred in 1 patient.

4. The diagnosis of true prostatic calculi by rectal examination can be made in relatively few instances. The only reliable method of diagnosis is the x-ray film. A plain film should be obtained in all patients with prostatic symptoms.

5. True prostatic calculi may be asymptomatic (17 per cent), cause mild symptoms (47 per cent), or produce moderate to severe symptoms (35 per cent).

6. The commonest presenting complaint of the patients in this series was some type of urinary dysfunction. Other symptoms included backache, suprapubic or perineal discomfort, pyuria, hematuria, and hemospermia. It is believed that in most cases the symptomatology is a reflection of the associated benign hypertrophy or prostatitis. Those patients with true prostatic calculi but without associated prostatic disease were usually asymptomatic or had very mild transient complaints. It is only in the infrequent case with very large and numerous prostatic calculi that the symptoms may be ascribed to the calculi per se.

7. In most patients with prostatic calculi, therapy is indicated primarily for the associated pathology in the prostate rather than for the calculi. In this series 35 per cent received no therapy, 43 per cent were treated with prostatic massage and medication and 22 per cent had surgery performed. A total of 78 per cent did not require any operative procedure.

8. Surgery was performed for two groups of cases; those patients with an associated prostatic hypertrophy of a sufficient degree to cause obstructive symptoms and those with very large and numerous prostatic calculi.

9. The choice of operative procedure depends primarily on the degree of enlargement of the associated prostatic hypertrophy. Transurethral resection is reserved for small glands that can be resected down to the capsule. Larger glands should be enucleated either retropubically or perineally together with excision of portions of the posterior prostatic capsule when indicated. In this series 5 patients had a transurethral resection and 5 patients had a retropubic prostatectomy and prostatolithotomy.

10. Case reports of 2 patients with giant false prostatic calculi are presented. In the first case, the calculus formed without previous prostatic surgery and replaced the entire prostate gland. It was removed perineally because of its partial position under the trigone and because of a markedly contracted bladder neck. The second case, a giant calculus formed in the prostatic bed several years following a suprapubic enucleation. This was removed suprapubically since it projected partially into the bladder through a wide bladder neck.

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THE INFRARED PHLEBOGRAM IN THE DIAGNOSIS OF BREAST COMPLAINTS

An Analysis of 1,200 Cases

LEO C. MASSOPUST and WESTON D. GARDNER, M.D.,
Milwaukee, Wisconsin

SINCE cancer propaganda is bringing more patients to the physician earlier in the course of the disease, it follows necessarily that the increased opportunity for the recognition of early mammary cancer offers a direct challenge to the medical profession, a challenge which must be met by new or improved diagnostic methods. Some of the new techniques have been helpful; however, a specific method is not yet available. Until a sensitive and selective diagnostic technique is found any method which has merit is useful as an aid in the differentiation of mammary diseases.

The present paper and its predecessors demonstrates that the superficial thoracic vein patterns in the female may be disclosed easily with a simple infrared photograph. Phlebograms of this area may be obtained without the introduction of a contrast medium by the simplest of photography.

In his preliminary report of an infrared photographic study of 100 cases of breast complaints, Massopust (3) shows that this method is helpful in differentiating some breast tumors. In a second publication, Massopust and Gardner (4) show that the normal pattern of the superficial thoracic veins varies extremely. This normal variation implies that there must also be a wide variation in the principal paths of venous drainage of the mammary glands. Batson proved that metastasis may occur through the venous system.

This report is an analysis of 1,200 infrared photographic studies of breast complaints correlated with the clinical and pathologic findings. The phlebographic studies were made by the authors in the Departments of Anatomy and Medical Photography of Marquette University School of Medicine. The clinical examination and the surgical and pathologic diagnosis were made by physicians and surgeons in private practice, the Cancer Detection Center of the Medical Society of Milwaukee County, and pathologists.

Ordinarily the photographic techniques and the method of evaluating the phlebogram would be omitted in a final report, but the interest and questioning encountered at recent meetings where this work has been exhibited indicate that a review of previous details of method is in order.

METHOD AND MATERIALS

The superficial thoracic veins lie within the depth of penetration of infrared radiation which is approximately 2.5 millimeters. These rays are absorbed either by tissue components of the veins or by venous blood. Consequently the remaining infrared radiation which is reflected to a camera produces an image on the emulsion which discloses the pattern of the veins.

The most convenient and efficient source of illumination for use with infrared sensitive emulsions is the incandescent tungsten filament lamp. Although this type of illumination requires a filter to be placed over the camera lens to exclude visible radiation, it permits positioning and photographing the patient in a lighted room. The patient stands before a dark background and is illuminated from each side by a vertical bank of five 100 watt lamps directed toward the chest. Two 500 watt lamps, 36 inches away at an angle of about 45 degrees are directed toward the chest. This angle will vary according to the

From the Department of Anatomy, Marquette University School of Medicine. This study was supported by a grant-in-aid from the Milwaukee County Chapter of the American Cancer Society.

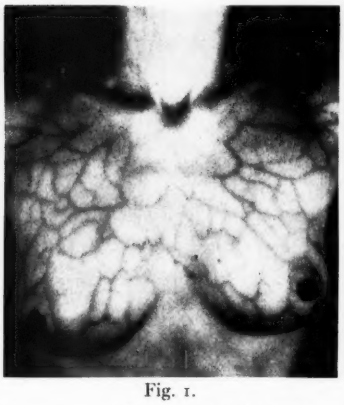


Fig. 1.

Fig. 2.

Figs. 1 and 2. Normal superficial venous patterns.

size and shape of the breasts. It is important to strive for flat illumination since very slight differences of light intensity are recorded with extreme contrast on the infrared sensitive emulsion. Movement is controlled by asking the patient to hold her breath. Two views are taken of each patient, one ventral view showing both breasts for comparison and a close-up view of the affected breast. If the complaint is in both breasts, close-up views are made of both. When indicated by symptoms of physical signs, lateral views of the breast or of the axillary region are made.

Any camera may be used but the larger type cameras yield better results without the loss of detail which is encountered in the enlargement of the rather coarse grained infrared film. The image is focused with a Wratten No. 25 filter placed over the lens. This filter is then replaced with a Wratten No. 87 filter and the diaphragm is closed to the *f*32 stop. The back of the camera is tilted slightly upward to bring the plane of the film parallel with the plane formed by the protruding breasts. This is particularly necessary if the breasts are large. The photograph is made on infrared sensitive film and the exposure time is ½ second. Infrared sensitive emulsions are loaded and processed in total darkness. Ordinary developers are used. The resulting negative may be studied like a roentgenogram using a view box, or contact prints may be made.

Since the photographic method is simple and very little special equipment is required, this technique can be used easily, quickly, and economically by the practitioner in his office. Groups, clinics, and laboratories with established photographic departments can add the method with ease.

INTERPRETATION OF INFRARED PHLEBOGRAM

In the second publication already mentioned, of Massopust and Gardner (4), the normally occurring extensive variations in vein patterns were analyzed and classified. These patterns form the basis of interpretation of the phlebogram of the diseased breast. Following the study of many infrared phlebograms, certain standards of interpretation were established. Only the pathologic results of many surgical cases will show how detailed the interpretation of the infrared phlebogram can be. This requires time, for a substantial number of cases in which the phlebogram was suspicious, neither biopsy nor surgery was suggested by the attending physician. The reading of the infrared phlebogram is based upon the following questions: (1) Are the mammary glands equal in size and uniform in shape? (2) Do the nipples point in the same direction? (3) Is there any dimpling or retraction in the breasts? (4) Is there retraction of the nipple? (5) Are the superficial veins distributed regularly and symmetrically over both pectoral regions and mammary glands?

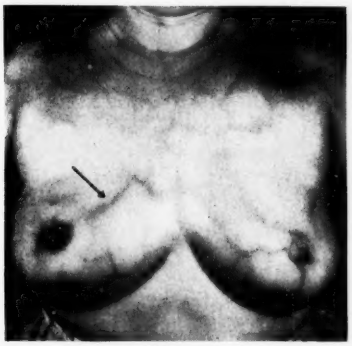


Fig. 3.

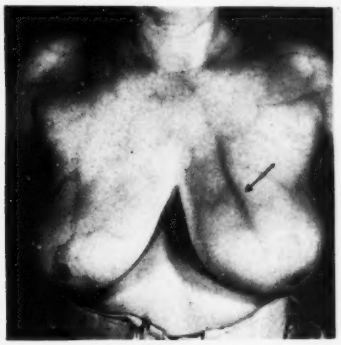
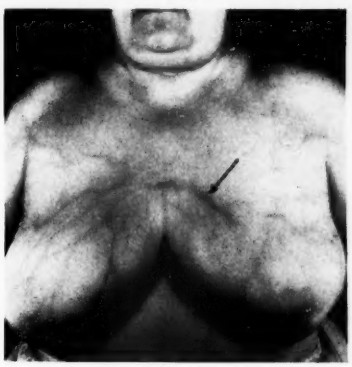


Fig. 4.



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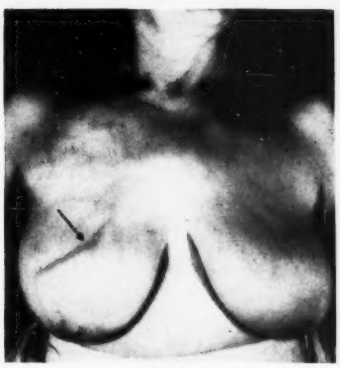

Fig. 6.

Figs. 3, 4, 5, and 6. Disturbance of the superficial venous pattern with engorgement of the principal mammary vein caused by malignant breast tumors.

(6) Are the veins more conspicuous on one side? (7) Are there areas of increased photographic density in the breast or in any of the veins of the thorax?

GENERAL FINDINGS IN NORMAL BREASTS

In addition to absence of alteration in form and contour of the breasts and nipples, there is symmetry in the venous pattern between the sides. The veins are uniform in size and photographic density and, in addition, are uniformly distributed. There are no areas of disruption of pattern or distribution. None of the veins appeared to be broadened, engorged, or tortuous (Figs. 1 and 2).

GENERAL FINDINGS IN MALIGNANT TUMORS

Symmetry in venous pattern usually is lost because, in the involved side, there is a disturbance or disruption of the venous pattern. Reference to the other breast discloses the pattern which might be expected to be present normally and indicates that there are veins apparently missing from the mammary plexus. This will be commented upon in the discussion. Certain of the remaining veins, or segments of them, in the pattern appear to be engorged. They are broadened, tortuous, and serpentine. There is an increase in photographic density and they give the appearance of having varicosities. The vein most frequently involved is the principal mammary vein which leads medially from the nipple or above it to the lower sternal region. This is a major vein in the drainage of the mammary gland and is a tributary to the anterior intercostal or internal mammary vein. This is particularly

Fig. 7.

Fig. 8.

Fig. 9.

Fig. 10.

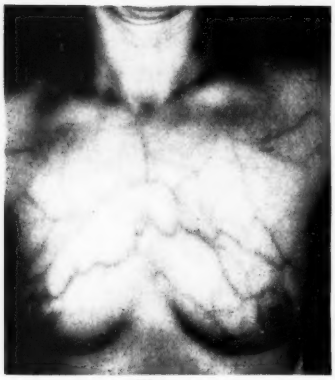

Fig. 11.

Fig. 12.

Fig. 7. Wrinkle below the left nipple with some engorgement of the veins at about 11 o'clock in an early malignancy.

Fig. 8. The principal mammary vein in the right breast is somewhat more conspicuous than that in the left; benign tumor.

Figs. 9, 10, 11, and 12. Deviation from normal patterns. Veins or segments of veins in one breast are more conspicuous than in the other.

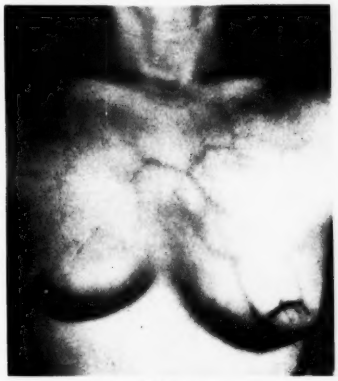

Fig. 13.

Fig. 14.

Fig. 13. Removal of 2 benign tumors caused asymmetry of the breasts and disappearance of some of the superficial veins in the right breast.

Fig. 14. Abnormal venous pattern. Disturbance and destruction of pattern in right breast, engorgement and tortuosity of a vein in lower sternal region and areas of increased photographic density.

vident in Figures 3, 4, 5, and 6. Slight rinkles or retractions which might be missed n inspection of the patient are visible beuse of the sensitivity of infrared film to ight differences in contrast (Fig. 7).

GENERAL FINDINGS IN BENIGN BREAST DISEASE

In their effect upon the venous pattern, benign tumors, cysts, abscesses, and fibrocystic disease may be grouped together. They do not produce a disturbance or destruction of the pattern nor alter symmetry between the two sides. There is uniformity of density and distribution. Engorgement, tortuosity, and serpentine changes are not seen. In a few of the benign cases the principal mammary vein was somewhat more conspicuous than that in the opposite breast (Fig. 8).

CLASSIFICATION OF PHLEBOGRAPHIC PATTERNS

Diagnosis was not attempted in the interpretation of the 1,200 phlebograms we have studied. Our routine procedure includes submitting a description of the phlebogram together with the photographs to the referring physician. The patterns are classified as follows:

1. Normal pattern (Figs. 1 and 2).

2. Deviation from normal pattern.—Veins or segments of veins, in one breast may be slightly more conspicuous than in the other, engorgement is not present; there is no disturbance of the pattern (Figs. 9, 10, 11, and 12). Surgery may also cause asymmetry of the superficial venous pattern (Fig. 13).

3. Abnormal pattern.—Symmetry has disappeared. There is disturbance or destruction of pattern, engorgement, broadening, and tortuosity of veins or segments of veins or areas of increased photographic density (Fig. 14).

DISCUSSION

The disruption and disturbance of the venous pattern which is seen in the phlebograms of the patients with malignant tumors give the impression that veins in the mammary plexus have been obliterated. Dissection of some of the surgical specimens shed no light on this subject because of the difficulty of attempting to trace the veins responsible for the pattern. The veins present were thin and collapsed and so friable that injection was fruitless. On the one hand, it may be that the malignant process actually invades and destroys veins along with other mammary tissue. On the other hand, the disappearance of veins from the pattern may be due to

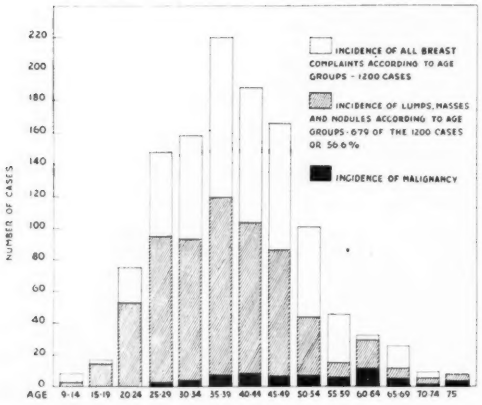
INCIDENCE OF ALL BREAST COMPLAINTS ACCORDING TO AGE GROUPS - 1200 CASES
INCIDENCE OF LUMPS, MASSES AND NODULES ACCORDING TO AGE GROUPS - 679 OF THE 1200 CASES OR 56.6%
INCIDENCE OF MALIGNANCY
NUMBER OF CASES
AGE 9-14 15-19 20-24 25-29 30-34 35-39 40-44 45-49 50-54 55-59 60-64 65-69 70-74 75

Fig. 15.

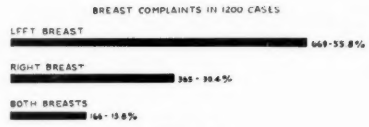

Fig. 16.

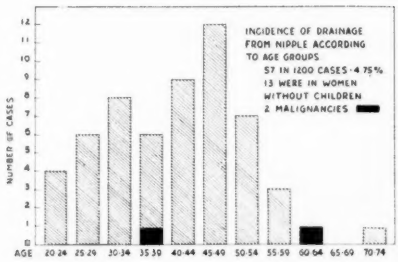
INCIDENCE OF DRAINAGE FROM NIPPLE ACCORDING TO AGE GROUPS
57 IN 1200 CASES - 4.75%
13 WERE IN WOMEN WITHOUT CHILDREN
2 MALIGNANCIES
NUMBER OF CASES
AGE 20-24 25-29 30-34 35-39 40-44 45-49 50-54 55-59 60-64 65-69 70-74

Fig. 17.

venous obstruction distal to the point of alteration in the pattern. The veins of this area would be collapsed and not visible by the infrared technique. If this were true, then broadening, engorgement, and tortuosity of remaining veins would be in compensation for veins collapsed due to obstruction.

None of the benign tumors showed destruction or disturbance of the superficial venous pattern. The greater conspicuousness of the principal mammary vein on the involved side in some cases of benign tumors is the principal finding in the "deviation from normal pattern" and suggests a transition form from "normal pattern to abnormal pattern." Since some investigators believe that previous mastitis and benign tumors are conducive to the development of cancer, it is possible that this conspicuousness of the principal mammary vein might be an indication of this tendency.

Garland has reported on the infrared venous patterns in 111 of his patients with breast complaints. These are included in the series being reported upon in this paper. He stated: "A normal venous pattern suggests that a lesion if present is benign but it may be present in malignancy. An abnormal pattern of the veins is commonly present in cancer, often present in benign lesions, and may be present with no evident disease. Differentiation between benign and malignant lesions cannot be made by this method."

We wish to emphasize once more that neither a diagnosis nor an opinion was offered on any of the phlebograms herein discussed. Garland, however, independently, classified his own cases which are included in our series, as normal and abnormal and failed to recognize a "deviation from normal" pattern.

We further point out that in our entire series, 5 cases which we classified as normal patterns were found to be malignant. One of these cases was that of a heavily pigmented negress in which the phlebogram revealed little of the venous pattern.

And again we point out that there were 12 cases in our series in which our interpretation of the phlebogram was not confirmed by the clinical diagnosis, but was confirmed by the final pathologic report of the microscopist. In 3 of these 12 cases the biopsy was negative, however, subsequent paraffin sections disclosed malignancy. We wish to emphasize also that in our 1,200 cases we have not found a single surgical case in which a benign tumor was associated with an abnormal pattern. Our results to date in precisely 800 cases in which follow-up has been complete show a statistical accuracy of 99.375 per cent.

Because statistical principles and methods have been quietly exercising their influence on thought and practice in medical research, various statistics are included in this report which perhaps are not directly pertinent to

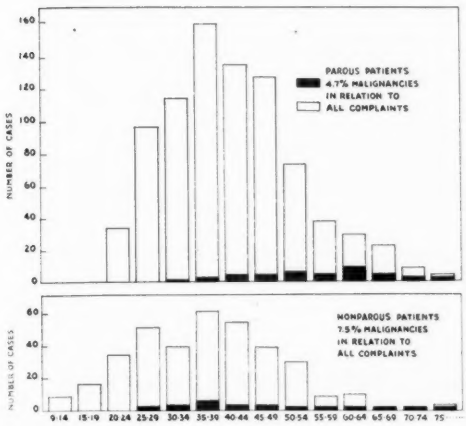

Fig. 18.

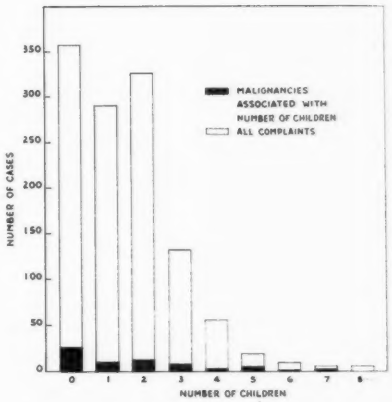

Fig. 19.

this study. However, we hope that they may be of interest and use to other investigators.

In Figure 15 statistics are presented upon the incidence of all breast complaints according to age groups. It will be noted that the greatest number of complaints is in the group between the ages of 35 and 39. In the same chart the curve of the incidence of lumps, masses, and nodules is almost identical with that of all complaints. In almost all of the patients in the age group between 60 to 64 years a lump, mass, or nodule was present in the breast, 40 per cent of which proved to be malignant.

The incidence of symptoms in the left breast was much greater than in the right as shown in Figure 16.

In all of the cases studied, 96.6 per cent were right-handed. However, in the left-handed group the number of complaints in the left breast predominated in about the same proportion.

Symptoms of drainage from the nipple were found in 57 patients (4.75 per cent), 13 of which were in nonparous women, as shown in Figure 17. Malignant disease was found in 2 of the 57 cases.

In our series of 60 malignant tumors of the breast, 2 patients gave a history of cancer in their family.

Of the 1,200 cases, 29.9 per cent were nonparous women. There were 15 malignant tumors in the 25 to 45 year age group as compared with 9 found in the same age group in the parous women, as shown in Figure 18. In the entire group of nonparous patients cancer was found in 7.7 per cent, while in the parous women it was found in 5 per cent. The incidence of cancer in the 45 to 60 year age group was 12.5 per cent in both parous and nonparous women.

The number of cancers associated with the number of children borne by the patient is shown in Figure 19. This shows a high incidence in the nonparous women.

SUMMARY

In the 1,200 cases studied, breast complaints consisted of: lumps, masses, or nodules in 679 instances; pain in 294; previous surgery for benign lesion in 60; routine check-up in 57; discharge from nipple in 57; previous surgery for malignant lesion in 15; mastitis in 24; and injury to the breast in 14 instances.

Follow-up examination in 195 surgical cases indicated: 101 instances in which the phlebograms were normal and the condition proved to be benign, 4 of which proved to be malignant; no instances of abnormal phlebograms in which the condition proved to be benign, 60 which proved to be malignant; and 30 deviations from normal phlebograms in which the condition proved to be benign.

Clinical diagnosis was made without surgery in 381 instances.

In 12 cases the phlebogram disagreed with the clinical diagnosis but was borne out by tissue studies.

CONCLUSION

It has been demonstrated that the infrared phlebogram can serve as an additional aid to the physician in the differentiation of breast tumors.

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CARCINOMA OF THE MALE URETHRA: ONE STAGE SURGICAL TREATMENT BY RADICAL PERINEAL EXCISION AND RECTAL TRANSPLANTATION OF THE DIVIDED TRIGONE

JOSEPH J. KAUFMAN, M.D., and WILLARD E. GOODWIN, M.D., F.A.C.S.,
Los Angeles, California

CARCINOMA of the male urethra, although uncommon, presents a serious urologic problem. Treatment is often unsatisfactory, and mortality s relatively great. McCrea and Furlong, in a ecent comprehensive survey, summarized reatment of this disease by stating that amutation of all or part of the penis appears to ive the best results. They concluded that masculation and x-ray therapy add nothing o life expectancy in these cases.

Cancer of the anterior urethra may be successfully treated by simple amputation, but he commoner and usually more extensive sions of the posterior urethra demand more adical surgery. Uhle and Holfelner have rently emphasized the need for surgical boldess in treating such tumors. Their case illustrates that the problems of reconstruction may be difficult.

Young's operation of segmental resection of the penis with shortening and reanastomosis is an ingenious contribution to the surgical treatment of carcinoma of the bulbous urethra. However, the extent of this insidious disease may preclude the use of Young's operation as in the case of Uhle and Holfelner and in our own experience. The surgeon should be wary of making the disease fit the operation rather than the operation fit the disease. The penalty of too conservative surgery is extension of the tumor and death.

The following procedure fulfills the objectives of wide surgical excision, comfortable urinary rehabilitation, and cosmetic appearance in the treatment of extensive carcinoma of the posterior urethra. It is done in one stage through a single perineal approach and safely allows preservation of the distal penis for purposes of ornament and sentiment.

From the Department of Surgery, Division of Urology, University of California, School of Medicine, Los Angeles, and the Section of Urology, Wadsworth Veterans Administration Hospital, Los Angeles.

OPERATION

The operation consists of radical excision of the proximal one-half or two-thirds of the penis with its crura and bulb, together with total prostatovesiculectomy. Effective and safe urinary control is achieved by transplantation of the divided trigone into the rectum.

Before operation the bowel is prepared for ureterointestinal transplantation (2). The patient is placed in the exaggerated lithotomy position and an inverted Y incision is made in the perineum (Fig. 1b). The midline incision is carried down to Colles' fascia, and by blunt and sharp dissection the penis is freed from the ischiopubic rami. This mobilizes the cavernous bodies anteriorly and the crura and bulb posteriorly. A clamp is placed under the cavernous bodies and their fascia, and the penis is transected at a point at least 2.5 centimeters distal to any palpable tumor. Gross evidence of carcinoma involving the urethra or corpora at this point demands transection further distally. The penis is then freed proximally from its attachments with a wide bloc excision limited only by the ischiopubic rami. The suspensory ligament is divided. The crura of the corpora cavernosa are isolated and divided close to the ischiopubic rami; and the bulb, bulbocavernosus muscle, transverse perineal muscles, and urogenital diaphragm are removed in continuity (Fig. 2). The arteries of the penis are divided and suture ligated next to the ischiopubic rami. When the membranous or prostatic urethra is

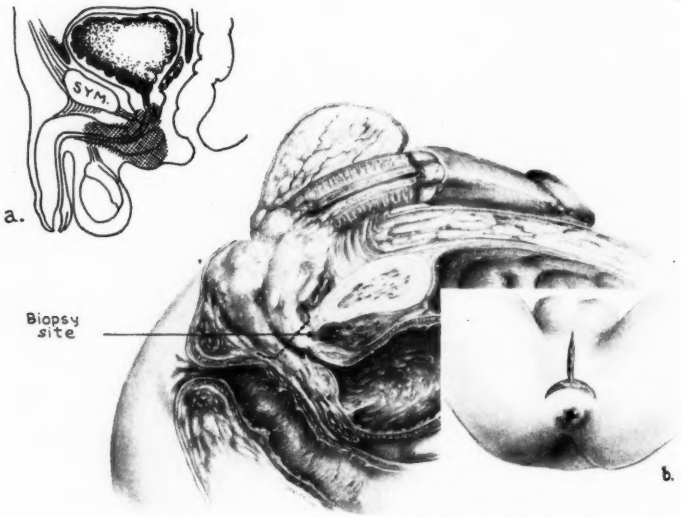

Fig. 1. Drawing of sagittal section of pelvis to show extent of the tumor (insert a) and type of perineal incision employed (insert b).

involved, prostatectomy is necessary in order to remove the tumor with a safe margin. Through the lateral limbs of the incision, the central perineal tendon is cut and the recto-urethralis muscle is included in the bloc. This leads to exposure of the apex of the prostate and Denonvilliers' fascia. The prostate, seminal vesicles, and bladder neck are then removed in continuity with the rest of the specimen (Fig. 2).

The excised specimen includes the proximal one-half or two-thirds of the penis with its surrounding superficial and deep fasciae, the bulb, bulbocavernosus muscles, transverse perineal muscles, crura of the penis with the ischiocavernosus muscles, Cowper's glands, the urogenital diaphragm, and the prostate, seminal vesicles, and bladder neck. A large defect is left in the perineum. The ischiopubic rami and pubis are cleanly exposed as are the levator ani muscles and the open bladder neck (Fig. 2b).

Reanastomosis of the distal penile urethra and bladder neck is impossible and would not provide urinary control. The exposure following bloc excision makes the trigone and rectum accessible for trigonal transplant through the perineal wound. Use of mucosa-to-mucosa anastomosis of the ureteral orifices to the rectum in application of the Maydl-Bergenhem principle for treating exstrophy of the bladder has previously been described in detail with Hudson (2). It is applied here as follows: The trigone is divided in the midline, and circular incisions approximately 1 centimeter in diameter are made through the mucosa around the ureteral orifices. Then a larger, 2 centimeter cuff of bladder including intramural ureter and ureteral orifice is developed on each side. Dissection is carried upward until the ureterovesical attachments are freed. The buttons of trigone and bladder wall containing intact ureteral orifices are implanted in the anterolateral walls of the rectum to produce anastomosis without tension. Temporary stay sutures are placed on either side of the proposed line of incision in the rectal wall, and the rectum is incised in two layers—a vertical seromuscular incision and a transverse mucosal stab. Anastomosis is done by suturing the bladder mucosa surrounding the ureteral orifice to the rectal mucosa with interrupted sutures of No. 0000 chromic catgut. A second layer of fine silk interrupted sutures unites the bladder muscularis to the rectal seromuscular layer (Fig. 3). Ureteral

Fig. 2. Drawing to show extent of surgical excision. Insert b shows appearance of the perineal wound after the tumor is removed.

Fig. 3. Drawing to show method of anastomosis of the divided trigone (see reference 2 for further details). Insert b shows closure of the bladder and the new position of the ureteral orifices low on the anterior wall of the rectum. Insert a demonstrates support of the stump of the remaining penis.

catheters are used during the anastomosis to facilitate the procedure but are removed when the anastomosis is complete.

The bladder neck is closed with chromic catgut. The distal penis attached only by its integument receives blood solely from the

Fig. 4. Right oblique urethrocystogram revealing destruction and filling defects from tumor in the posterior urethra.

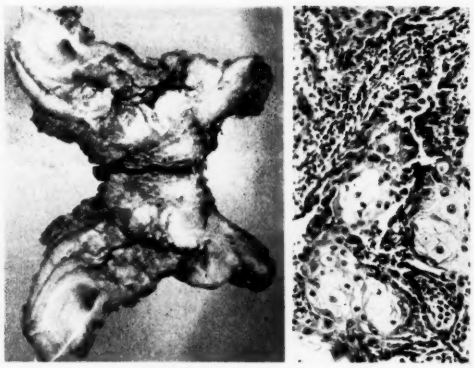

Fig. 5. a, left, Sagittal section of surgical specimen. Bulbous urethra is to the left; prostate to the right. b, right, Microscopic appearance of tumor.

superficial skin vessels; yet this allows its preservation. Buck's fascia is closed over the exposed corpora and urethra. The stump of the penis is then attached to the periosteum of the inferior aspect of the pubis (Fig. 3a). Penrose drains are placed to the region of the bladder neck and in the perineal space. The levator ani muscles are approximated in the midline, and the perineal body is attached to the inferior pubic arch. After the skin is closed, a large mushroom catheter is placed in the rectum and sutured in place for urinary drainage.

Postoperative care is similar to that for any ureterointestinal transplant. The rectal tube may be left in place until the patient is ambulatory, and drains are gradually shortened.

CASE REPORT

P.K. (WGH No. 31016), a 57 year old white cook, entered the hospital with a 7 month history of dysuria and a 6 month history of a tender perineal mass. Prior to his admission, biopsy of the perineal tumor performed by a colleague revealed grade II squamous cell carcinoma of the urethra. Suprapubic cystostomy had been performed for relief of severe obstructive symptoms. There was no history of gonorrhea or urethral stricture.

The patient was found to have a firm, fixed, tender perineal mass 5 centimeters long and 3 centimeters wide. The mass could not be felt on digital rectal examination, and the prostate was of normal consistency and mobility. The suprapubic tube drained purulent urine, and Bacillus proteus was recovered on urine culture. A bloody, purulent urethral discharge was present. Nodes were not palpably enlarged. Laboratory studies were normal.

Chest films and excretory urograms were negative, and no evidence of bony metastases was seen on roentgenographic survey. Urethrograms revealed an irregular dilatation extending 6 centimeters in the bulbomembranous urethra (Fig. 4). Urethroscopy confirmed these findings, and the tumor appeared to extend proximally to a point just below the verumontanum. The bladder was free of tumor.

Young's operation, segmental excision of the tumor followed by reanastomosis, was originally planned in this case. However, the degree of involvement and extension proximally made such a procedure inadequate. Following a 6 day period of bowel preparation, the operation described was done on March 4, 1952. The penis was transected in its midscrotal region, and no evidence of tumor was seen. Biopsy just below the triangular ligament revealed gross and microscopic evidence of tumor extending upward into the apex of the prostate. Total prostatovesiculectomy was done in an effort to remove all carcinoma (Fig. 5).

The problem arose as to the best way to manage urinary diversion. Three possibilities were weighed: closure of the bladder neck with permanent suprapubic cystostomy, conventional transabdominal ureterosigmoidostomy either at this time or at a second stage, and transplantation of the divided trigone to the rectum. The exposure following the extensive resection appeared to favor the last mentioned, and previous favorable experience with this type of anastomosis induced us to try it here. The transplant proved to be time consuming and difficult technically because of the depth of the wound, but a satisfactory anastomosis without tension was achieved. The operating time was 5½ hours. The stump of the remaining distal penis was sutured to the inferior pubic arch as described earlier. It was believed that should the penis fail to remain viable, it could be amputated subsequently with ease.

Urinary output through the rectal tube was good from the first postoperative day. On the third post-

operative day a leak through one or both anastomotic sites was evidenced by the drainage of large amounts of urine through the perineal wound and the suprapubic cystostomy. Gentle suction was applied to a small catheter placed in the perineal wound which gradually became dry. When the rectal tube was removed on the tenth postoperative day, the patient passed stool and urine per rectum with good anal sphincter control. The suprapubic catheter was removed 3 weeks postoperatively, and the suprapubic fistula and perineal wound were healed and dry on the twenty-fourth postoperative day. Excretory urograms on the thirtieth postoperative day revealed no evidence of dilatation of the upper tracts and no extravasation at the sites of the anastomosis (Fig. 6). The patient's blood chemistry studies remained normal throughout the postoperative course. One year postoperatively the patient was well and had no complaints. However, he would not return for examination or x-ray study, and no venture can be made regarding his cure.

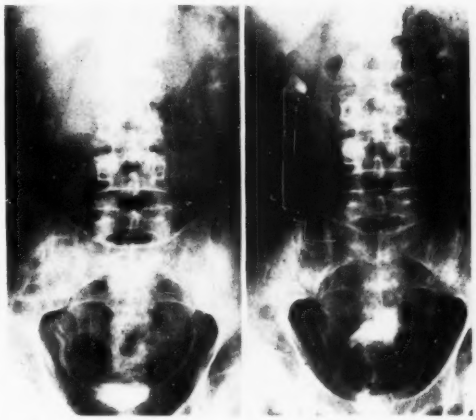

Fig. 6. Intravenous urograms. a, left, Preoperative; b, right, 1 month postoperative.

DISCUSSION

Since McCrea and Furlong have recently reviewed all proved cases of carcinoma of the male urethra from 1861 to 1950, it is not necessary to discuss the disease in detail here. There are several aspects of the surgical treatment of carcinoma of the posterior urethra which deserve emphasis. The disease is often insidious in its development and may remain undetected for long periods. Delayed diagnosis and incomplete removal of the lesion probably account for the high mortality rate associated with the disease. Definitive cancer surgery must have as its primary goal complete extirpation of the tumor. Reconstruction necessarily assumes a secondary role, but mutilation should be avoided wherever possible.

The operation described here is believed to fulfill these objectives. It is a somewhat arduous technical procedure, and familiarity with the anatomy of the perineum is important. The trigonal transplant to the rectum through the perineal wound must be done without optimal exposure. The method of vesicorectal transplantation described by Boyce and Vest for exstrophy of the bladder might also be applicable but would be no easier from a technical standpoint.

The distal pendulous portion of the penis can apparently remain viable even after its primary blood supply has been interrupted. In the case presented, the appearance and color of the penis and glans remained normal throughout the postoperative course. Preserving the "external" penis seems desirable from both cosmetic and psychologic standpoints, and its amputation adds nothing to the radical aspects of the operation. Emasculation is not necessary.

Pelvic and groin lymphadenectomy is still a moot question in the treatment of carcinoma of the urethra. Many urologists believe that it is probably not indicated in the absence of palpable inguinal glands. Ureterointestinal anastomosis done through an abdominal incision may seem more desirable to some urologists than the transplant described here. One advantage of the abdominal operation is that it provides opportunity to ascertain the presence of iliac gland or abdominal metastases. However, the primary echelon of metastases from cancer involving either anterior or posterior urethra is the inguinal nodes. In 17 patients with carcinoma located in the posterior urethra in whom data regarding metastases were available, McCrea and Furlong found the inguinal nodes involved in 10. There were 11 cases with distant metastases and none of these were found to have had iliac glands involved primarily. Hence it would appear that in the absence of palpable superficial nodes and in the absence of x-ray findings of distant metastases, there is little

to be gained by abdominal exploration. When distant metastases are undetected and the primary tumor is too extensive for Young's operation, the operation described provides relief from the misery that these patients may ultimately suffer as a result of the primary growth.

Although the operation described here is difficult, its obvious advantages justify its use in such cases as this. The ureterointestinal transplantation is extraperitoneal, low in the bowel, and it preserves the ureteral orifice and its intrinsic valve-like action. It is advantageous to the patient and the surgeon to achieve definitive treatment in a single operation.

Although this operation is limited in application, it is presented because it is basically sound and deserves additional trial and evaluation.

SUMMARY AND CONCLUSIONS

1. Carcinoma of the posterior urethra in the male challenges adequate surgical removal and satisfactory urologic rehabilitation.

2. Young's operation is ideally suited to tumors of the bulbous urethra but should not be applied to large lesions which involve the prostate and membranous urethra.

3. An operation which is done through a single perineal approach is presented. It fulfills the requirements of wide excision, satisfactory urinary diversion, and freedom from disfigurement.

4. The operation embodies radical resection of the proximal one-half or two-thirds of the penis with its adnexae, the triangular ligament, prostate, and seminal vesicles.

5. Rectal transplantation of the divided trigone through the perineal wound provides optimal ureterointestinal urinary diversion.

6. The distal penis deprived of its primary blood supply can survive as a result of the rich vascular endowment of its skin attachments. Its preservation is cosmetically desirable and does not compromise the primary aims of the operation.

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EXPERIMENTAL REPAIR OF EXSTROPHY OF THE BLADDER WITHOUT CYSTECTOMY BY USING A FREE FASCIAL GRAFT

ALEXANDER C. BARET, M.D., WILLIAM E. DEMUTH, JR., M.D.,
JOHN J. MURPHY, M.D., and MARK W. MUIR, M.D.,
Philadelphia, Pennsylvania

THE rehabilitation of patients with exstrophy of the bladder presents a problem as yet unsolved. In the past 100 years there have been in excess of 70 different operations proposed for its correction, and more than 400 articles devoted to exstrophy of the bladder have been published. For the past several decades the generally accepted and usually employed procedure has consisted of transplantation of the ureters into the large bowel, excision of the exstrophied bladder, and reconstruction of the genital defects. The transplantation of ureters into the large bowel leaves much to be desired. In a recent critical review of the faults of ureterosigmoidostomy, Creevy points out that the four principal dangers which may be incurred are: direct ascent of bacteria from the bowel up the ureters, intracolonic pressure forcing intestinal contents into the ureters and renal pelves, stenosis of the anastomoses, and hyperchloremic acidosis, the last mentioned being reported in as high as 79 per cent of patients following ureterocolic anastomosis. It has also been shown that periureteral lymphatics do convey bacteria toward the kidneys.

In Smith's series of 66 ureterointestinal anastomoses for causes other than exstrophy of the bladder, 9 died of "renal failure" within 2 years of operation, and renal disease was a serious problem in 18 of 54 surviving patients, a 33.3 per cent morbidity. The only large group of cases of exstrophy of the bladder followed for a long interval after repair was reported by Harvard and Thompson. They traced 128 patients who were operated on in the conventional method as stated. There were 144 patients initially, 18 of whom were surgical deaths, half of which were attributed to pyelonephritis. There were 27 deaths due to renal failure, and pyelonephritis was responsible for 65.7 per cent of all late deaths. Excretory urograms were used to study 41 patients from 6 months to 35 years after operation, and only 5 patients or 12.2 per cent were found to have urographically normal kidneys.

One positive fact emerges, and that is the longer the survival the greater the renal morbidity. In 1934 Walters and Braasch reported 85 cases of exstrophy treated by the Coffey-Mayo ureterosigmoid transplant technique and stated that only 13 patients survived beyond 10 years. Indeed, Boyce and Vest in a searching analysis of the problem remark that of the many hundreds of children treated for exstrophy in the past 50 years "there is not one report in the medical literature of one of these attaining a normal life expectancy." In their approach to this problem they circumvented the necessity for direct ureteroenteric implantation by first giving their 2 patients a permanent colostomy; then after sterilizing the isolated rectosigmoid pouch with antibiotics, they inverted and closed the bladder after creating a vesicoenteric fistula. They thus obtained a sterile urine reservoir having anal sphincteric control, and they predict a normal life expectancy for the 2 patients so treated.

A major factor in the problem has been the presumed necessity of excising the remaining bladder. If the bladder could be preserved and restored to functional use the disastrous sequelae of ureteral transplantation to skin or bowel could be avoided, at least in part. The late Hugh Young who was in avid search of

From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, Philadelphia.

Fig. 1.

Fig. 2.

Fig. 1. Total defect of abdominal wall created by excising all layers. Prevesical fat and superior portion of bladder visible. Due to tissue retraction wound measures 6 by 9 centimeters.

Fig. 2. Entire anterior half of bladder has been resected down to the vesical neck. Hemostasis has been secured with fine silk ligatures.

Fig. 3.

Fig. 4.

Fig. 3. Posterior bladder wall sutured to peritoneum, fascia, and skin with chromic No. 0 catgut. Operation completed. Vesical neck visible at inferior border of exteriorized bladder.

Fig. 4. Exteriorized bladder seen 2 weeks after picture in Figure 3 was taken. Bladder has healed well in place. Ureteral orifices clearly seen as projecting papillae.

such a solution just prior to his death was able to rehabilitate successfully a 6 year old girl with exstrophy of the bladder by inverting and closing the remaining viscus. Then by a series of plastic procedures he formed a urethra with sphincteric control. Sweetser, also, has advocated plastic reconstructive efforts in bladder exstrophy and he reported a 6 months old male patient in whom repair was accomplished by a modified Burns technique. Although Sweetser and Burns have been able to conserve and close the exstrophied bladder in their single cases, Young's patient is apparently the only one reported in American urologic literature in whom continence was obtained.

Fig. 5. Anterior rectus sheath fascial autograft about 5 by 7 centimeters applied to freed up bladder and sutured on with muscle side out. A No. 20 French wing tip soft rubber catheter inserted down through the urethra before closure.

It is well known that large segments of the bladder may be excised without greatly diminishing the eventual capacity of the viscus. Presumably, the remaining portion of the detrusor is capable of functional dilatation of remarkable extent. The experiments described here were designed to take advantage of this faculty of the bladder, together with some phenomena observed in the course of other experiments with fascial grafts used by other investigators in repairing artificially created bladder defects.

METHOD

Artificial exstrophy was produced in 9 female dogs ranging in weight from 32 to 46 kilograms by a method somewhat similar to that described by Maluf and Pilcher and associates for other purposes. The method was modified to include resection of part of the abdominal skin and wall. Thus, a portion of each rectus together with the skin overlying and the peritoneum beneath was excised to create a defect in the anterior abdominal wall similar to that seen in the naturally occurring congenital abnormality. Approximately half of the dome and the entire anterior portion of the bladder was excised. The edges of the bladder were sutured to the peritoneum, rec-

tus fascia, and skin by means of a continuous suture of chromic No. 0 catgut. No dressings were used and the animals were returned to their cages without special attention.

After a period of 3 to 4 weeks surgical repair of the created exstrophy was carried out. A sheet of rectus fascia about 5 by 7 centimeters was taken from the anterior rectus sheath through an upper abdominal incision. The edges of the bladder were separated from the fascia and skin and the entire bladder was freed up except in the region of the vascular pedicles and ureters. The fascial graft was placed on the bladder, muscle side out, and the edges of the graft were sutured to the muscle and mucosa with a continuous suture of chromic No. 0 catgut. A second suture of plain catgut, size 0, was placed to overlap the vesical serosa and fascia. The graft thus replaced the previously excised anterior half of the bladder.

Just prior to closure of the newly formed viscus a No. 18 French rubber catheter was passed down through the vesical neck, out through the urethra, and into the vagina where it was sutured into place. However, the sutures in the vagina proved too irritating, and the first 5 dogs operated on all succeeded in removing the catheters within a few days. The last 4 dogs were put on bladder drainage by inserting a No. 20 French wing tip soft rubber catheter from above and cutting it off short in the vagina. Closure of the suture line was completed, the bladder was placed in the peritoneal cavity, and the fascia and skin closed over it, the latter being undermined when necessary. The catheter was left in place 10 days, unless sooner removed by the animal.

Figures 1 to 5 show the steps outlined in creating and repairing the bladder exstrophy in dog 306.

RESULTS

It is significant that 4 of the first 5 dogs developed urinary fistulas which had to be excised, while none of the last 4 dogs on better controlled bladder drainage developed any fistulas.

Dogs were studied by cystograms, observation of voiding patterns, and gross and microscopic examination of the bladders after sacrifice. Kidneys were grossly normal when examined post mortem. Bladder capacity was estimated at the time cystograms were made.

Fig. 6. Excised bladder of dog 73, anterior surface showing. Note that graft area lies centrally and more to the left. Dog sacrificed 52 days after insertion of fascial graft; 65 centimeters of water placed in bladder.

With the dogs under nembutal anesthesia cystograms were made by instilling 5 per cent silver iodide emulsion through a No. 20 French Foley catheter which was first used to empty the bladder. The first cystograms were taken 31 days after excision of the fistulas in 3 dogs and 162 days after repair of the exstrophy in dog 1394. Anteroposterior and lateral films

TABLE I

Dog No.	Cystogram 1		Cystogram 2	
	Catheterized urine c.c.	AgI emulsion c.c.	Catheterized urine c.c.	AgI emulsion c.c.
284	25	35	30	70
533	90	90	30	90
853	0	40	50	100
1394	40	50	40	90
Controls				
69	50	120		
70	50	120		
73	0	120		

Fig. 7.

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 11.

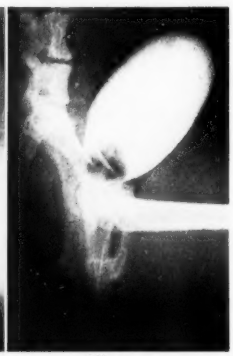

Fig. 12.

Figs. 7 and 8. Anteroposterior and lateral views of bladder of dog 853. Bladder capacity estimated to be 40 cubic centimeters 2 months previously. With this second cystogram bladder capacity was 100 centimeters. Compare to normal bladder in Figures 11 and 12.

Figs. 9 and 10. Anteroposterior and lateral views of bladder of dog 1394. Capacity at time of first cystogram 2 months previously was 50 centimeters. When this cystogram was made capacity was 90 centimeters. Note irregular contour of bladder at graft site which has obviously shrunk.

Figs. 11 and 12. Anteroposterior and lateral views of bladder of normal dog, No. 69, with 120 centimeters of 5 per cent silver iodide emulsion instilled. Note the outline of the Foley catheter.

were made. One dog developed a recurrent fistulous tract, and due to the extent of granulation and scar tissue formation, and partial sloughing of the graft, it was not further utilized in the study. Table I shows the results of 3 cystographic studies, the second performed 57 days later, and a third of 3 controls. It will be noted that in the second cystogram 3 of 4 dogs had about doubled their bladder capacities within 2 months.

The criteria used for ascertaining capacity were a slightly visible, distended bladder with the dog supine, and a feeling of resistance to further influx of the radio-opaque emulsion which was added very slowly through the Foley catheter by using a 20 cubic centimeter glass syringe. The bladder volumes so obtained probably fall between absolute and functional capacities. By using identical technique in 3 control animals of similar size and weight, the criteria for bladder capacity were met during influx of the last 5 cubic centimeters of emulsion.

Repeated observation of the voiding patterns of the first 4 dogs in the series revealed a good force of stream and no unusual frequency during the month or so preceding sacrifice. In 7 cases the dogs voided shortly before sacrifice, and no residual urine was found in the bladder. One dog, No. 73, agonally micturated an estimated 100 cubic centimeters. A picture of the excised bladder of this dog is shown in Figure 6 with the anterior surface up.

Representative cystograms are shown in Figures 7 to 10. A control is shown for comparison in Figures 11 and 12.

When excising the bladders it was noted that the graft site was almost invariably fixed to the prevesical fat or to the abdominal wall. However, this did not appear to affect bladder function in any way. It was estimated that

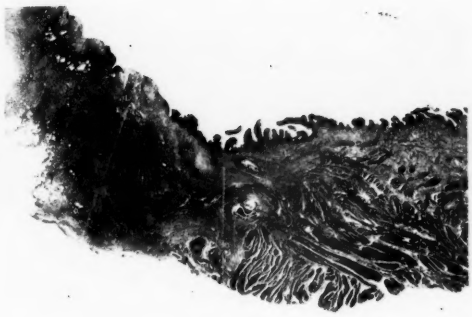

Fig. 13.

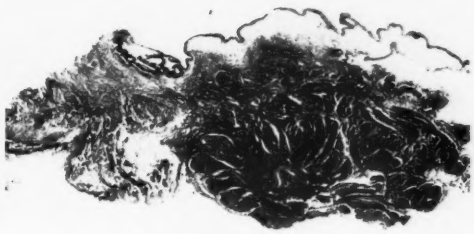

Fig. 14.

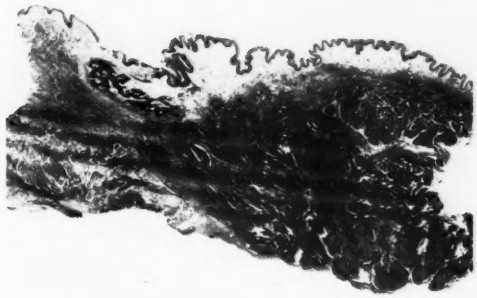

Fig. 15.

Fig. 13. Photomicrograph of section of bladder of dog showing junction of fascial graft and normal bladder. Dog sacrificed 14 days after insertion of graft. Epithelium migrating out over fascia.

Figs. 14 and 15. Sections from bladder of dog 73 whose intact bladder is shown in Figure 6. Dog was sacrificed 52 days after insertion of graft. Epithelization apparently complete. Note small islands of osteoid bone formation.

the grafts had shrunk by approximately 50 per cent but more accurate estimation was impossible due to the lack of a line of demarcation between bladder and graft.

Examination of the bladder mucosa revealed what grossly appeared to be intact epithelium in 4 dogs sacrificed from 194 to 238 days, and in 1 dog sacrificed 52 days after application of the graft. Four of 8 graft sites were found to have small plaques of bone 1 to 2 millimeters thick and varying in area from 3 by 3 millimeters to 7 by 10 millimeters.

Sections for microscopic study were taken through the graft areas and included normal bladder. Four dogs sacrificed 194 to 238 days after repair showed complete epithelization. Small areas of osteoid bone formation occurred in 2 cases underneath intact epithelium. Dogs sacrificed at shorter intervals showed varying degrees of epithelial migration over the graft tissue. Thus, dog 306, sacrificed 14 days after repair, showed healthy graft tissue with transitional epithelium growing out over it for several millimeters, as shown in Figure 13. Dog 73 whose bladder is shown in Figure 6 was sacrificed 52 days after insertion of the fascial graft. Figures 14 and 15 show two sections of the graft area enlarged approximately 10 times. Epithelization appears to be complete. A small area of osteoid formation has occurred just beneath the migrated epithelium.

Other investigators who have used free grafts of rectus sheath or fascia lata in repairing defects in the ureter, bladder, stomach, and bowel reported successful epithelization of the graft in almost every instance. Rates of epithelization are not reported, but Neuhof stated that it is "complete early," while Lord and his associates reported 13 of 14 successful

cases of complete epithelization in ureteral tube grafts 1 to 2 centimeters long. DeMuth reported complete epithelization in 120 to 180 days over grafts 3 centimeters in diameter placed in 4 dog bladders, but in 1 case found no epithelium over a small area of bone formation.

DISCUSSION

It would appear that successful restoration of the exstrophied bladder, whether by the method used by Hugh Young or by the employment of free fascial grafts, has much to commend it, especially when one considers the high mortality where no surgical intervention has occurred and where cutaneous or bowel implantation of the ureters has been carried out. It must be emphasized that this is a preliminary study dealing primarily with the feasibility of reconstructing the exstrophied bladder by using free fascial autografts of fairly large size. Only part of the problem is thus dealt with, for repairing the invariably associated genital defects and securing urinary continence provide the other major tasks in completely rehabilitating such individuals. Further studies are planned in which the artificial exstrophy will include defects in the vesical neck and the roof of the posterior urethra of female dogs.

Although small areas of osteoid bone formation have a tendency to occur in some of the grafts, Neuhof did not believe that these would interfere in any way with bladder function, and, indeed, our observations bear this out. No calculi were found in any of the bladders. The matter of bone formation and why it occurs are still a matter of conjecture. It probably can best be related to the presence of fibroblasts and the common embryonal origin of fibrous connective tissue and bone.

The utilization of free fascial autografts for the repair of bladder and other visceral defects has been advocated by Kirschner, Neuhof, DeMuth and others. These investigators have shown that even in aseptic fields the grafts take well and in addition can sustain tension. Indeed, Kirschner, after excising an exstrophied bladder, repaired a 10 by 12 centimeter defect of the entire abdominal wall which was soiled by urine and feces. Although after skin mobilization, a 4 by 10 centimeter area of fascia lay exposed, it did not necrose or herniate. Numerous investigators have amply demonstrated that the abdominal defects in cases of bladder exstrophy can be readily repaired by sliding or free fascial autografts. Among the advantages of using fascial autografts are their ready availability, their tendency to heal in place, the minimal blood supply required for their nourishment, their great tensile strength, and the ease of their adaptability to the surface of any organ.

SUMMARY

It has been demonstrated that exstrophy of the bladder is a congenital anomaly of serious consequence which greatly compromises the life expectancy of the person so afflicted, whether left untreated or corrected surgically by conventional ureteral transplantation procedures. The necessity of excising the bladder is questioned. A restoration of the viscus by the use of free autografts of anterior rectus sheath fascia is proposed. This technique might also be useful in the surgical repair of traumatic bladder injuries and wide segmental bladder resections.

Such a procedure has been successfully used in 8 dogs in which the entire anterior half of the bladder and dome was excised and the remaining portion exteriorized. In a second operation the defect was repaired with a fascial autograft measuring about 5 by 7 centimeters in size, obtained from the anterior rectus sheath. Four dogs were followed by cystograms and when compared to 3 controls their bladders were shown to have undergone a gradual increase in size and capacity toward the control volumes, although the grafts had shrunk by 50 per cent. Voided urine was clear and force of stream was good. Histologic sections showed a tendency toward early epithelization of the fascial graft and some evidence that the process was completed by 2 months. In 4 of 8 dogs small areas of bone formation occurred in the graft tissue without apparent effect upon the integrity of the graft, bladder function, or completeness of epithelization. Calculus formation was not observed. At the time of sacrifice kidneys were grossly normal.

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EDITORIAL

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NOVEMBER, 1953

ABUSE OF RADIATION THERAPY

INJURIES have been known to follow excessive exposure to radium or roentgen rays for many years. In spite of these known dangers, the total number of cases of chronic radiation dermatitis and necrosis appears to be on the increase. In spite of this knowledge and in spite of repeated teachings the repair of injuries of this nature continues to be one of the major items on the practice of all plastic surgeons. It is not a subject of local importance but one of international scope. These complications frequently produce tragic results, not only as local deformities, but many patients are driven to morphine addiction in their relief from the pain and itching that is ever present. Also, many developmental deformities are seen following irradiation over the epiphysis of growing children, a resultant growth arrest thus being produced. More therapeutic treatments are being given, some by trained radiologists and dermatologists, but unfortunately also by the general practitioners who have been "sold" an x-ray machine by the salesman. The latter has never failed to point out the large variety of diseases which the practitioner could treat with it, but he himself probably knew less of the dangers involved than the doctor purchasing it. Other injuries arise following overzealous treatment of cutaneous lesions that might well have been treated more judiciously by adequate surgery. Many surgeons, uncertain whether or not their surgery has been adequate, will advise postoperative x-ray therapy in addition. Postradiation complications frequently occur as a result of treatment by conscientious physicians who have not been trained properly in the administration or who are not aware of the hazards involved. Severe damage may arise following treatment of a person who is unusually susceptible or from the effect of an x-ray machine that has not been properly calibrated. Patients may receive radiation therapy from several individual physicians, without each succeeding therapist bothering to learn how many roentgen units have been given before. Since only a maximum total can be tolerated over a given area irrespective of the time lapse between treatments, the net total under these circumstances is frequently sufficient to produce injury. I have been deeply impressed by the observation of several patients who have received radiation therapy over 50 years previously, only to have breakdown and carcinomatous degeneration occur after this long interval. Such observations are not surprising, however, when one remembers that the endarteritis of the underlying vessels is an irreversible process, and this, plus normal arteriosclerotic changes in the vessels, is bound to result in a state of diminished local nutrition so that breakdown becomes inevitable. Con-

versely, I have seen 1 patient who developed squamous cell degeneration of an acute x-ray ulcer within 6 months after excessive therapy to a simple basal cell carcinoma of the skin over the ankle.

However, in comparison with the vast number of treatments given with roentgen and radium rays, the actual total of injuries is relatively small. But to the plastic surgeon who sees this group of patients the number seems entirely too large. Because of this one cannot stress too highly the seriousness of the problem.

The severe pain and itching are well known subjective symptoms of chronic radiation dermatitis. Permanent alleviation cannot be obtained until all of the damaged tissues have been excised. Following radical excision, complete symptomatic relief is dramatic and permanent. Cure can then be anticipated as soon as the defect created by the surgical excision has been closed.

Objectively, one will note atrophy, telangiectasia, and some minor contractures of the skin. As found in other cutaneous lesions associated with avascularity, chronic ulceration and carcinomatous degeneration are not infrequent. Our own cases show that over 50 per cent have degenerated into squamous cell carcinomas. Undoubtedly this figure would even be higher if the chronic radiation ulcers were permitted to remain for longer periods of time without excision. We have 1 case in which the lesion degenerated into a spindle cell sarcoma.

The pathologic changes are routinely typical. The essential finding is an obliterative arteritis or hyalinization of the vessels in the damaged area. This is an irreversible obliterative process that is seen in arteries, veins, capillaries, and lymphatic vessels which together produce interference in nutrition of the affected tissues. White necrosis or anemic gangrene occurs eventually which finally results in ulceration. The area is left with poor circulation which becomes worse with the passage of time. A gelatinous membrane develops over the painful ulcer. The surrounding tissues become fibrotic and if of sufficient magnitude may extend into the adjacent muscles, tendons, and bone. Telangiectasis, pigmentation, atrophy, thickening, and keratosis develop, the rate of progress being dependent upon the degree of arteritis present. Finally, many chronic lesions, as stated heretofore, degenerate into squamous cell carcinomas.

When one considers the progressive avascularity produced in the pathogenesis of a radiation injury, it becomes obvious that there is little place for conservative management of this lesion. In spite of enthusiastic reports given by advocates of local application of radon paste or the aloe vera leaf, we have yet to see any patient who has ever responded permanently to such simple management. Successful permanent cure can be anticipated only when all damaged tissue has been excised back into an area of good blood supply. This level is sometimes difficult to estimate but one should always err on the side of being too radical. If the excision is not wide enough, future reconstructive operations will fail, since later degeneration will occur around and below the site of original excision.

Reconstruction of the excised defect calls for considerable judgment and experience on the part of the surgeon. A small defect can sometimes be closed by primary suture of its borders. A wound in which there is a subcutaneous fat pad with adequate blood supply can usually be covered with a free skin graft. But because of the avascular nature of defects of this type and because adequate excision has left exposed tendons, nerves, bone, or large blood vessels in its bed, some type of pedicle flap containing both skin and subcutaneous fat will frequently be found necessary in order

that a well nourished final covering can be obtained. But more important than treatment of chronic radiation ulcers is their prevention. True enough, cancercidal doses must be given in order to effect a cure of certain types of deep seated cancer. The late development and treatment of these lesions is acceptable when a cure of the original malignant growth has been accomplished. But far more important is the intelligent management of many cutaneous lesions. Most of them can be completely cured if adequate primary excision is carried out. The average cutaneous cavernous hemangioma for instance is rarely very vascular. Hence its surgical removal is both safe and simple. The reconstruction of the resulting surgical defect is no problem in the hands of surgeons doing that type of work. Basal cell epitheliomas of the skin can likewise be cured by surgical excision as well as by radiation therapy. However, if the skin cancer does not become cured after a legitimate amount of radiation therapy has been given, this type of treatment should be stopped at once and surgical removal carried out. Postoperative x-ray therapy is never indicated if adequate primary excision has been done. And finally, if any radiation therapy is indicated, it should always be given by a well trained expert.

PAUL W. GREELEY.

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THE BOOK SHELF

THE FIRST APPENDECTOMY

PHILIP G. CREESE, M.D., Reading, Massachusetts

"When the doctor is in doubt and the patient in danger, make an exploratory incision and deal with what you find as best you can."

LAWSON TAIT, after Kronlein (26)

TO THE modern surgical world, the name of Claudius Amyand, Principal Surgeon to St. George's Hospital, London, has no significance, yet the fame of this 18th century surgical pioneer should have been guaranteed by his report of the first recorded appendectomy, published in the *Philosophical Transactions of the Royal Society* in October 1736, under the rather prolix title: "Of an Inguinal Rupture, with a Pin in the Appendix Coeci, incrusted with Stone; and some Observations on Wounds in the Guts," by Claudius Amyand, Esq., Serjeant-Surgeon to His Majesty, and F.R.S. (5).

The story of this operation is best told in Mr. Amyand's own words, for he has a colorful manner of writing and the language of the period enhances this. To continue:

"October 8, 1735. Hanvil Anderson, a Boy, 11 Years of Age, was admitted into St. George's Hospital near Hyde-Park Corner, for the Cure of a Hernia Scrotalis, which he had had from his Infancy, and a Fistula between the Scrotum and the Thigh terminating into It, which for a Month last past had discharged a great Quantity of an unkindly sort of Matter. The Rupture was small, and not troublesome, and Part of it could be replaced, but as it appeared that the Sinuous Ulcer sprung from that Part that could not; so t'was evident that the Cure of the Fistula depended upon the Cure of the Hernia, which latter could be obtained by no other Operation than that for the Bubonocele, which was agreed to, and performed the 6th Day of December following.

"This Operation proved the most complicated and perplexing I ever met with, many unsuspected Oddities and Events concurring to make it as intricate as it proved laborious and difficult.

"This Tumour, principally composed of the Omentum, was about the Bigness of a small Pippin: In it was found the Appendix Coeci perforated by a Pin incrusted with Stone towards the Head, the Point of which having perforated that Gut, gave way to a Discharge of Faeces through the fistulous Opening therein, as the Portion of the Pin obturating the Aperture in it shifted its Situation. The Abscess formed in the Hernial Bag occasionally, and the Suppuration for two Months last past from this place outwardly, had knit and confounded, and, as it were, imbodied together the Gut and the Omentum with the Hernial Bag, and these with the Spermatick Vessels and the Testicule, so that it was difficult to distinguish them from each other, as it was to separate them without wounding them; this Pin, whose Point was fixed in the Omentum, continually shifting its Situation, and occasioning a Discharge of Faeces. The Pin frequently lying in the way of the Knife, and starting out of the wounded Gut, as a Shot out of a Gun, the Inundation of Faeces upon this Occasion from a Gut we could not well distinguish, were so many Difficulties in the way: But the greatest yet was, what to do with the Gut, which all this while was unknown, and of which we could not come to the Knowledge, till the Operation was over; for this Appendix Coeci, which was the only Gut found in the Rupture, was so contracted, carnous, duplicated, and changed in its Figure and Substance, that it was impossible to determine what kind of Gut it was, or to find out that it was only this Appendix elongated, and in Disguise.

"We apprehended none of these Difficulties, when we undertook this Operation, in which we proceeded as usual: The Omentum lying uppermost in the Hernial Bag was dissected from the Parts it was knit to, and particularly the Gut it was imbodied with, and afterwards cut off close to the Abdominal Muscles without any previous Ligature, the Vessels in it being small, and the substance of it more like a Sweetbread than the Caul.

"Much Time was spent in this dissection; we were straightened for Room, and greatly disturbed by the Discharge of Faeces coming out of the Gut, upon every Motion the Pin lodged in it and the Omentum suffered, upon the separation of these from each other. The Gut forming a double Tube, like a double-jointed Syphon, continuing in the Curve as it passed over the Testicule and Spermaticks, was separated one part from the other and the adjacent Parts, as far as the Aperture in the Abdominal Muscles, where the unperforated End of it was separated therefrom, and thence stretched out and unfolded, which brought in View the Aperture made in it by the Pin hitherto concealed, through which that Part of it, which was incrusted with Chalk, had just made its way out upon an occasional Pressure, as a Cork out of a Bottle. It was the opinion of the Physicians and Surgeons present, to amputate this Gut: To which End a circular Ligature was made about the found Part of it, two Inches above the Aperture, and this being cut off an Inch below the Ligature, was replaced in the Abdomen, in such a manner that an artificial Anus might be made there, if the Pa-

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VIII. *Of an* Inguinal Rupture, *with a* Pin *in the* Appendix Cœci, *incruſted with Stone*; *and ſome Obſervations on* Wounds *in the* Guts; *by* Claudius Amyand, *Eſq*; *Serjeant Surgeon to His* MAJESTY, *and F. R. S.*

October 8, 1735. *Hanvil Anderſon*, a Boy, 11 Years of Age, was admitted into St. *George's Hoſpital* near *Hyde-Park* Corner, for the Cure of a *Hernia Scrotalis*, which he had had from his Infancy, and a Fiſtula between the Scrotum and Thigh terminating into it, which for a Month laſt paſt had diſcharged a great Quantity of an unkindly ſort of Matter. The Rupture was ſmall, and not troubleſome, and Part of it could be replaced, but as it appeared that the Sinuous Ulcer ſprung from that Part that could not; ſo 'twas evident that the Cure of the Fiſtula depended upon the Cure of the Hernia, which latter could be obtained by no other Operation than that for the *Bubonocele*, which was agreed to, and performed the 6th Day of *December* following.

This Operation proved the moſt complicated and perplexing I ever met with, many unſuſpected Oddities and Events concurring to make it as intricate as it proved laborious and difficult.

This Tumour, principally compoſed of the Omentum, was about the Bigneſs of a ſmall Pippin: In it was found the Appendix Cœci perforated by a Pin incruſted with Stone towards the Head, the Point of which having perforated that Gut, gave way

Fig. 1. First page of Amyand's paper describing the first successful appendectomy on record. The significance of the paper is somewhat clouded by the length of the title (5, p. 329).

tient's Case should require it. Afterwards so much of the Hernial Bag as had been detached from the Skin, the Spermaticks, etc. was cut off, which, as they appeared in a sound State, were preserved in Situ. The Fistulous Opening adjoining to the Thigh, and answering to the Aperture in the Gut, was opened; some Angles of Skin in the way removed; The Aperture in the Muscles, which had been inlarged by Incision, was stopped up with a Tent; and the rest of the Dressings and the Situation of the Patient ordered so, as to remove from the Wound all such Pressure from within as might disturb the Cure.

"'Tis easy to conceive that this Operation was as painful to the Patient as laborious to me: It was a continued Dissection, attended with Danger on Parts not well distinguished: It lasted near half an Hour, and the Patient bore it with great Courage. During it the Patient vomited largely, and had several Stools, but was soon composed by half an Ounce of Diacodium and Emollient Embrocations and Fomentations, frequently applied warm on the Belly: He was blooded, and an Emollient Carminative oily Clyster was ordered to be applied in the Evening; but as he was easy, and the Belly not Tense, that was omitted."

Although the surgeon says that he took a long time, almost half an hour, the speed of the operation seems remarkable to us. Undoubtedly poor Hanvil thought otherwise. The patient was dressed on the fourth postoperative day, everything was in order and he was having normal bowel movements.

Mr. Amyand continues:

"The Tent put into the Abdominal Aperture was not removed until the 8th. Upon the 10th the Ligature around the Appendix Coeci, where it had been amputated, dropt off, and no Faeces followed it; . . .

". . . During the Time of the Cure he was confined to his Bed, always kept to sparing Diet, and ordered never to go to Stool but in a Bedpan; by these means the Wound was completely healed up in less than a Month, and the Patient soon after discharged with a Truss, which he was ordered to wear some Time, to confirm the Cure.

"That the Appendix Coeci should be the only Gut found in this Rupture, is a Case singular in Practice: This was full of Excrements, and occasionally could be distended with an additional Quantity, which upon Pressure was returned into the Colon, with that kind of Noise which Guts replaced generally give. . .

"The Patient does not remember, when he swallowed the Pin which had perforated the Gut within the Rupture. But as this Rupture was from his Infancy, fixed and unreducible, so it is likely the Pin had then made its way into the Appendix Coeci prolapsed; and that an Inflammation ensuing thereon, had occasioned an Adhesion, whereby the Increase of the Tumour had been checked, and the Reduction of the Parts prolapsed thereby, rendered impracticable.

"The Patient also perfectly remembers, that the Impostumation or Gathering preceding the fistulous Discharge was attended with very little Pain, or much less than generally attends Suppuration."

Thus, the remarkable story of the first appendectomy on record. Amyand had regrets afterward and said that Nature would probably have cared for it by having the pin work its way out. What is not surprising, the rupture recurred. The surgeon said that this is the third or fourth case in which the operation for rupture failed! However, he adds, "the operation is more effective for hernia than the Caustick, or any other method."

Amyand sent the surgical specimen to the Repository of the Royal Society, but sad to relate, it is no longer in existence. The Museum of the Royal Society was turned over to the British Museum in the 18th century and inquiries there report that it is lost (32).

HISTORY OF APPENDECTOMY

The history of appendicitis and appendectomy is filled with contradiction and confusion as to the priority in making a surgical attack on the organ. Because of this confusion, an attempt

should be made to put the facts in order, so that credit may be properly given and that an oversight in medical history may be corrected, if only for reasons of scholarship. A brief review of the history and documentation is required.

Many authors have given credit to Mestivier of France who in 1759 published a report of a case he had done at the Hospital St. Andre de Bourdeaux in 1757. He presented a case of an abdominal abscess in a 45 year old man, which he incised and drained, removing about a pint of pus. The wound drained for a long time and when almost healed, the patient died. Autopsy showed a gangrenous appendix with an encrusted pin in it. I believe it important to note that Mestivier merely drained the abscess, he made no attempt to remove the appendix and apparently had little idea at the time of surgery that the appendix was the site of disease. Furthermore, he had a most unsuccessful outcome. Yet this is the report that is repeatedly described in the literature as the classic case of the first operative attack upon the appendix.

Twenty-two years before this, Amyand in London had not only removed an appendix, also with a pin in it, but what is more, his patient recovered. For some unknown reason Mestivier's report found its way into history, while Amyand's description was buried in obscurity. Major and Garrison both cite Mestivier. Edebohls who reviewed 2,500 articles on appendicitis for his paper on the history of the disease also gives credit to Mestivier and does not mention Amyand. The frequently quoted paper of F. Melier of France, writing in 1827, presented a classic on the significance of the appendix and its diseases. Melier (citing Wegeler) says that the case of Amyand was the only one that was similar to his autopsied cases. Despite the fact that Melier is quoted in almost every article on the history of appendicitis, this reference to Amyand almost entirely escaped notice.

There are some who might say that Amyand does not deserve credit since he was operating for a hernia and accidentally came upon the involved appendix with a pin in it, a most rare occurrence. But if Mestivier is to be given priority, certainly Amyand has a far stronger claim. The early history of appendicitis is centered almost exclusively around foreign bodies in the appendix. The next 3 cases reported, all from France in the next 50 years were similar (1). Mahoney in 1921 found reports of only 40 pins in the appendix in 160 years. The mortality rate for these before 1895 was 72.2 per cent. Amyand was indeed more fortunate than he realized!

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Cicatrix, effectually to ſecure the Patient againſt a Rupture. During the Time of the Cure he was confined to his Bed, always kept to ſparing Diet, and ordered never to go to Stool but in a Bed-pan; by theſe means the Wound was completely healed up in leſs than a Month, and the Patient ſoon after diſcharged with a Truſs, which he was ordered to wear ſome Time, to confirm the Cure.

That the Appendix Cœci ſhould be the only Gut found in this Rupture, is a Caſe ſingular in Practice: This was full of Excrements, and occaſionally could be diſtended with an additional Quantity, which upon Preſſure was returned into the Colon, with that kind of Noiſe which Guts replaced generally give. This had occaſioned a Diminution of the Tumour when compreſſed, before the Operation was performed, as the Patient was lying backwards with his Head downwards, and an Increaſe of it as he ſtood erect, when the Fæces from the Colon could get into it again.

The Patient does not remember, when he ſwallowed the Pin which had perforated the Gut within the Rupture. But as this Rupture was from his Infancy, fixed and unreducible, ſo it is likely the Pin had then made its way into the Appendix Cœci prolapſed; and that an Inflammation enſuing thereon, had occaſioned an Adheſion, whereby the Increaſe of the Tumour had been checked, and the Reduction of the Parts prolapſed thereby, rendered impracticable.

The Surgeons who conſtantly dreſſed the Patient before the Operation, did obſerve then, as they have ſince, that the Humour diſcharged formerly at the Fiſtula, had frequently the Appearance, and, as they thought,

Fig. 2. Amyand recognizes that he has performed a unique operation, though he is quite unaware of the importance of what he has done (5, p. 333).

The appendix in a hernial sac was described a number of times in the early period of appendectomy (18). It is of unique interest that the first appendectomy performed in the United States by Hall at the Roosevelt Hospital, New York, in 1886 was done after a hernial sac was entered for what was apparently a strangulated hernia. He found an abscess with a gangrenous appendix, which he removed (35, 41). Thus the first case of appendectomy ever reported and the first case in the United States were for rather bizarre, though almost identical forms of appendicitis.

Kronlein in 1884 is credited by some (19, 36) with the first appendectomy, but here again the preoperative diagnosis was not made and the

patient who had a perforated appendix with peritonitis expired. Groves of Ontario (24) in 1883 and Symonds of London (39) in the same year also have been given the honor of the first appendectomy, but it has been shown that Amyand predated them by almost one and one-half centuries! It was only through the thorough scholarship of John B. Deaver that Amyand's name has survived at all in the modern surgical literature. Others (21, 27) who credit him with priority are only citing Deaver. It is perhaps possible at this late date to correct the records of medical history and give to Claudius Amyand the place which he deserves.

Here, let us quote from Deaver: "That a knowledge of the pathology of the vermiform appendix slumbered, nay, even hibernated, from the time of Melier (1827) (who cites the work of Amyand 92 years earlier) until the day of Fitz, is one of the most remarkable things in the whole history of medicine. . ." (17).

BIOGRAPHY OF AMYAND

Since our surgeon has remained in limbo for more than two centuries, it is perhaps only proper that something should be known of the life of this rather remarkable man. Amyand was not a surgeon with only one blade for his scalpel, but a person who accomplished much in one field and another throughout a full and busy life. Let us look at the record and see with whom we are dealing in the year 1735. At that time Amyand was Principal Surgeon, along with Ambrose Dickins and William Cheselden, to the staff of St. George's Hospital in London. In addition to their staff positions, they also served on the Board of Governors. Cheselden was surgeon to Queen Caroline and was one of the most famous surgeons of his day. Ambrose Dickins had been apprenticed to Claude Bernard and had married his daughter. Succeeding Bernard on his death, he had the unusual distinction of serving as Sergeant-Surgeon to three monarchs, Queen Anne and Kings George I and II. Claudius Amyand was also Sergeant-Surgeon to King George II, a position of distinction and responsibility. Amyand had also been Master of the Barber-Surgeons Company in 1731, a singular honor (37).

So here we find our pioneer surgeon, no unknown then, but a man in his early fifties, full of honors, "one of the most distinguished surgeons of his day" (44), at the apogee of his career. His accomplishments would seem to have been sufficient to guarantee him his little niche in history, had he never done an appendectomy. But we find that neither his more worldly successes nor his scientific deeds sustained him. Peachey, a thorough scholar, says: "In compiling biographical memoirs of the early surgeons to St. George's, one meets with little assistance from the printed records. . . Further, it was quite exceptional in that period for a surgeon to possess a degree, . . . Cheselden, Hawkins and Bromfield alone have been deemed worthy of a place in the *Dictionary of National Biography*. Memoirs of the two Sergeant-Surgeons, Dickins and Amyand—unaccountably missing from that Dictionary—are to be found in Mr. Sidney Young's *Annals of the Barber Surgeons*." Neither Peachey nor Young knew of Amyand's priority in appendectomy, but based their evaluation on his other accomplishments.

If Claudius Amyand had not had a son who was knighted and thus entered in *Burke's Peerage* most of the biographical facts about him would have been completely lost. Only by this circumstance was it possible that such information should be available. Claudius was the second son of Isaac Amyand, a Huguenot refugee who fled from Marnac, Xaintonge, France after the Revocation of the Edict of Nantes and was naturalized in London in 1688. Isaac and his wife, Anne Hottot, had 7 sons and 2 daughters. Claudius was born in Paris, he was naturalized in London on April 11, 1700, but prior to this had received the sacrament, according to the usage of the Church of England on February 18, 1700. These are the only data which give a clue as to his age, for according to the Acts of Parliament (1 Wm. & Mary. C. and 9. Wm. III. C.20), all persons naturalized under these Acts should take the sacrament within 5 years of their attaining the age of 14, it would thus seem that Claudius was born between 1681 and 1686 (38).

There is nothing known of Claudius in the years immediately after 1700, when he must have been serving his apprenticeship. If we presume that he was 16 years old in 1700, he probably was put out to a surgeon, as was the custom. Conjecture is substituted for fact here, but it is known that Ambrose Dickins and Amyand were the closest of friends. Dickins was approximately the same age as Amyand, having been born in 1687 (47). Dickins was apprenticed to Claude Bernard, Sergeant-Surgeon to Queen Anne, for a period of 7 years and in 1709 was admitted to the Freedom and Livery of the Barber Surgeons. When Bernard died in 1710, Dickins succeeded him as Sergeant-Surgeon at the early age of 23. (How different from today's specialty boards!) Thus, although I can find no mention of it, there

certainly is a great probability that both Dickins and Amyand were apprenticed to Bernard, for later their careers and friendship, almost absolute parallels, suggest a common bond.

For a time, however, their careers diverged. Amyand went to the wars in Flanders and was a participant at the Battle of Blenheim on August 13, 1704. He must have been still an apprentice surgeon at this time for he was only about 20 years of age. He received 30 pounds as his share of the bounty from this battle (25). Between 1704 and 1708 we again lose track of Claudius; it is possible that he returned to England for a while in those years, but later returned to Flanders since we find him in the British Army at Ghent in 1708. From there he reported on: "A Relation of an Idiot at Ostend, with two other Chirurgical Cases," in a letter to a Mr. Wilson on January 30, 1708. This letter was read to the Royal Society by Mr. de la Fage and reported in the *Philosophical Transactions* (2). Even as a neophyte surgeon of 24, Amyand was observing and reporting what he saw. It is probable that Amyand participated in the campaign that led to the Battle of Oudenarde in 1708, resulting in a victory for Marlborough.

It is possible that he met George Lewis of Hanover during this latter campaign, this Prince of an insignificant German realm, later to be George II of England? The future George II served as a volunteer under Marlborough at Oudenarde and distinguished himself by leading a cavalry charge in the battle (15, 28).

In any event, Amyand was commissioned sometime before 1715 as Surgeon of Lumley's Horse, the First Dragoon Guards, and he maintained his interest in the military for years after; his commission was renewed on June 20, 1727, to continue until July 10, 1739. In 1722 he was granted an annual pension of 200 pounds per year for his services (25).

After 1708 nothing more is heard of Claudius, until 8 years later when he was elected a Fellow of the Royal Society on April 5, 1716, at the age of about 32, certainly an honor for one so young. It is more than likely that he had established himself in surgical practice in London during these years and was getting on quite well, defying the adage: ". . . it has been usefully observed that the English physicians seldom get their bread till they have no teeth to eat it" (37). At least he was in a suitable position to wed Mary Rabache on November 5, 1717 and then proceed to raise a family of 3 sons and 6 daughters.

In the 1720's there was a political, intellectual, and scientific ferment which centered about the Royal Court. "In the future George II the King (George I) possessed an heir as stupid as has ever reigned in England, while Caroline, Princess of Wales, was to become her ablest Queen. Her the King merely termed a she-devil, but for the Prince he shared the feelings of His Russian Majesty, who slew his son, and of His Prussian Majesty, who proposed to follow that example. In London, however, a royal father could only break off intercourse, and even this was now formally resumed" (14).

But the future Queen was more than a "she-devil," for she was one of the few "enlightened" souls who patronized science and the arts at the Court of George I (45). In 1721 Lady Mary Wortley Montagu introduced smallpox inoculation into England (46). Princess Caroline and Lady Mary were friends. Caroline had almost lost Princess Anne from the disease and when smallpox broke out in London in 1721 she greatly desired to protect Princesses Carolina and Amelia from its ravages. She persuaded George I to allow experimental inoculation on 6 condemned felons, on condition that they should be pardoned afterward. Five of the criminals contracted the disease in mild form and recovered, the sixth concealed previously having smallpox and so was not infected—they all escaped hanging in any event. Then Princess Caroline carried the experiment further and had 11 children from the charity ward of the Parish of St. James inoculated by Mr. Amyand, and it too proved successful. On April 17, 1722, the Princesses Carolina, aged 9, and Amelia, aged 11, were inoculated by Claudius Amyand under the watchful eye of Sir Hans Sloane, the Royal Physician (37, 45). The inoculations, fortunately for Claudius, turned out a success. That Amyand had great courage is attested by this act alone, for despite the patronage of these high circles there was a tremendous opposition to the practice, although: "Before the introduction of inoculation, smallpox killed one out of four of those whom it attacked; that method changed it into a disease by which only one out of several hundreds perished" (29, p. 182).

Amyand carried on despite the opposition, for we find: "During the first 3 years of the practice 477 persons were inoculated in Great Britain, of whom 9 died, and 29 did not receive the infection—a mortality in 3 years of 2 per cent: the principal inoculators in England being Dr. Nettleton in Yorkshire, 80 patients, Mr. Amyand, Serjeant-Surgeon, 62, and Mr. Maitland, 85" (37, from Sloane Ms., 406B, fol. 17). There is a list of 21 persons inoculated by Claudius Amyand

in or about London during the year 1728. All of these were people of good position, most of them children of the nobility of tender years; all but one (aged 11 weeks) had the smallpox and recovered. Amyand is a man to be remembered for these contributions alone. It is odd that there are no known papers by him on the subject, he liked to report the new and unusual. Possibly he thought there was enough controversy raging and that he had better leave such matters to the ladies, i.e. Caroline and Lady Mary, who seemed better suited to violent crusading, as only ladies can be when aroused. Possibly he considered himself too much the surgical specialist to concern himself greatly with an essentially medical problem.

In 1728 Mr. Amyand and Mr. Dickins were appointed Sergeant-Surgeons to King George II, George I having died the previous year. Dickins had served in this position since 1710, but, although Amyand treated the family of the Prince of Wales in 1722, there is no clear record that he was Surgeon to George I. It is more likely that he was Surgeon to the Prince, until the Accession when he was made Sergeant-Surgeon.

That the office called for special consideration at the time of Amyand is attested by the fact that on May 7, 1728 Mr. Amyand was "admitted to the freedom of the Barber-Surgeons, examined and approved touching his skill in surgery, admitted to fine for all offices to the Parlour door, and elected on to the Court of Assistants. It was ordered on the same day 'in regard to the dignity of their offices' that Mr. Serjeant Dickins and Mr. Serjeant Amyand should hereafter take precedence next after the Governors for the time being" (47). It seems strange that Amyand should not be a member of the Barber-Surgeons until 1728, for his great and good friend Dickins was admitted in 1709. However, his rise was rapid, for he was Warden in 1729 and 1730 and was Master of the Company in 1731, succeeding Dickins in these offices. It was not until some years later, in 1745, that the Barbers and the Surgeons separated by Act of Parliament (18 GII).

And what of the royal patient? It has been said that he was stupid, but others had a different opinion. Lucas says: "He (George II) was by no means a cipher. He had high spirit and great energy. He was certainly master in his own house, and he flattered himself that he was actually ruler of his kingdom. But although he was something of an egoist and autocrat at home, he was not conceited or obstinate enough to insist upon introducing that spirit into all affairs of State" (28, p. 94). The King, though devoted to Caroline was not above a bit of extracurricular activity. He called on Mrs. Howard (later Lady Suffolk) each night at nine and spent 3 or 4 hours with her. "She was the only attraction which took him away from his wife" (28, p. 21).

Amyand must have had a rather difficult position at times for we find that: "Amongst other imaginary accomplishments he (George) prided himself, like many conceited people, on his knowledge of medicine: the Duke of Newcastle wrote to his brother that 'the King is a bit of a doctor' . . ." (28, p. 22). However, there may have been some recompense for: "George hated illness: he never would allow that he was ill himself, nor tolerate illness in others. The Queen, in an attack of gout, would soak her aching feet in cold water, so that she might get on her boots in time to go walking with him" (28, p. 21).

Fortunately for the Sergeant-Surgeon, George appears to have remained in rather good health. Amyand served the King until his own death, when he was succeeded in the appointment by the notorious John Ranby (23). It was he whom Queen Caroline, with her usual perspicacity called "the blockhead," just before submitting to an operation by him for a strangulated umbilical hernia, from which she died (40, 42).

That Mr. Sergeant-Surgeon Amyand was something more than a journeyman practitioner may be appreciated by his activities in still another sphere. In the early part of the 18th century the population of London consisted of some 1,000,000 souls, yet there were only two general hospitals in the entire city, St. Thomas's and St. Bartholomew's. The Westminster Hospital was opened in 1721, Guy's in 1724, and St. George's in 1734. Claudius Amyand was appointed the first Principal Surgeon of Westminster on November 8, 1721, being joined by Dickins in the next month, and later by Cheselden. These men served without pay or reward of any kind, since the hospitals were founded primarily as charities; they certainly set a high standard of selfless devotion, for the demands on the surgeons' time were often great.

"There were two classes of surgeons; the first three noted in the list (Westminster Staff), Amyand, Dickens, and Cheselden appear to have performed the chief operations, but the dressings were left to the surgeons of the neighborhood whose names are often mentioned incidentally in the Minutes" (44).

And as always: "Among the surgeons themselves there were degrees of social status, the

Fig. 3. Site of the first appendectomy. Originally Lanesborough House, it was leased by Amyand and his colleagues after the schism with Westminster Hospital and as St. George's Hospital began to receive patients in 1734.

Mr. of the ordinary surgeon comparing unfavourably with the Esq., which was the prerogative of the Serjeant-Surgeon, those attached to the households of the lesser members of the Royal Family, and those who held appointments to the Forces" (37).

Affairs at Westminster went along smoothly until 1733, when the great controversy broke out. The buildings of the hospital in Chapel Street were in precarious condition, a committee was appointed of which Mr. Amyand was a member. It was proposed that a number of houses in James Street and Castle Lane be taken over, having been offered by Mr. Green, a vice-president of the Charity. Part of the committee was against this proposal and wished to select an entirely new site. The dissenters were a minority of the committee, but they certainly were a high-handed lot, for while the controversy was as yet unsettled they leased Lanesborough House in Hyde Park on September 20, 1733 for 7 years. Drs. Stuart, Wasey, Teissier, Sergeant-Surgeons Dickins and Amyand, and Mr. Thomas Smith signed in trust for the new society which they had set up, yet they were all on the Westminster Staff at the time and comprised the principal physicians and surgeons of the staff. They made an offer of Lanesborough House to the Westminster Directors, but were refused and thereupon submitted their resignations in October 1733, leaving the hospital practically unstaffed. Sergeant-Surgeons Amyand and Dickins were requested to continue to attend on patients on extraordinary occasions, to which they consented. Cheselden resigned, but was appointed a Consulting Surgeon and continued in the hospital.

The new hospital at Lanesborough House provided for 60 patients, but the grounds and buildings were such that expansion could be easily accomplished. On October 19, 1733 the first General Board Meeting of St. George's Hospital was held and Mr. Sergeant Amyand and Mr. Sergeant Dickins were appointed Principal Surgeons, later Mr. Cheselden was added. The staff promised to serve without fee or reward of any kind. The Principal Surgeons were not allowed to have pupils or apprentices, as were the surgeons-in-ordinary who obtained some income in this way. The hospital began to receive patients in 1734 and by 1735 had to enlarge to 100 beds and needed more.

It is of passing interest to note that: "It was ordered that a limited number of beds should be provided with straps and handcuffs, 'for use in the same manner as at the Westminster Infirmary,' the cost of each set being 13s. These were probably used for operations (especially those of cutting for stone), which, until the provision of an operating theatre in 1745, were performed in the wards or the surgery (OPD)" (37). The effect on the morale of other patients must have been quite striking under these conditions, especially when anesthesia was as yet unheard of. We can well imagine the scene from the description of the operation on poor Hanvil Anderson.

St. George's prospered and grew rapidly, but again there arose dissension. On December 16, 1737 Sergeant-Surgeon Dickins presented complaints to the Board of Governors against two surgeons-in-ordinary, Wilkie and Hawkins. The details are not known, but there was a discussion

concerning experimentation and malpractice, Dickins came off second best in the argument, for the Board would take no action. On December 21, 1737 Dickins and Amyand handed in their resignations as Principal Surgeons, these were accepted and they were given a vote of thanks for their services. No further Principal Surgeons have ever been appointed at St. George's, these two were made Consulting Surgeons on February 3, 1738 and this title has persisted through the years.

Amyand and Dickins were extremely resentful as a result of this dispute, they induced some of the supporters of the hospital to withdraw their support, amongst these was the Earl of Burlington, a heavy contributor.

One would gather from their behavior that both Dickins and Amyand were proud, headstrong individualists who would go their own way if the world would not go theirs. One good result of their stubbornness was the founding of St. George's, today one of the great London hospitals—so even recalcitrance may have virtue.

Claudius Amyand throughout his professional life recorded and reported on strange and unusual cases which came to his attention, he produced no book, nor did he ever thoroughly explore a subject; this would seem to fit with the personality of the man. He was an active doer, a man of affairs, rather than a profound scholar, and as a scientist he was fundamentally a reporter, but one who based his opinions on what he learned at autopsies. He does exhibit in his writings a sound surgical judgment, which would stand today. That he was interested in natural phenomena and took delight in things scientific is attested by his early election to Fellowship in the Royal Society—an active, vigorous, and select group under the leadership of Sir Hans Sloane, its first physician President, and including amongst its members at the time Sir Isaac Newton. A perusal of the *Philosophical Transactions of the Royal Society* of that day shows its members to have been in correspondence with the most learned minds in Europe and America, the first stirring of the scientific age can be noted here.

Amyand contributed 9 known papers and reports to the *Transactions* between 1708 and 1746, although he died in 1740. Editorial efficiency was not so highly geared in the 18th century as it is today and papers were often published 5 and 6 years after they were delivered at the dinners of the Royal Society at Pontac's in Abchurch Lane. It is strange that a scholar of Peachey's caliber should say that Amyand was not credited with any published work; again Fate seems to have been against Claudius.

Briefly, his papers in the *Transactions* were:

1708 (2)—The results of an autopsy on an idiot of Ostend who was found to have a tremendous quantity of hardware in his stomach. He also reported on a large tumor of the femur in a child, and a depressed skull fracture in a soldier.

1732 (3)—On a congenital abdominal hernia in an infant. Of a hematocolpos causing urinary retention, with operation and cure. Of an autopsy on a girl which revealed an asymptomatic hourglass stomach.

1735 (4)—An Autopsy on a young man in good health, until just before death, who was found to have a large patent foramen ovale of the heart.

1736 (5)—In the paper on appendectomy, he also reported on the autopsy of a soldier who had an appendix located in a hernial sac. Amyand was apparently aware that the appendix had some pathologic significance, but he never came to grips with the problem.

1738 (6)—He tells of a huge cholecystic abscess which he drained, death resulted 3 weeks later. The liver appeared normal, the gallbladder was dilated to the point where it could hold 3 pints of fluid. The common duct was patent.

1738 (7)—Of a strangulated hernia of 6 days' duration attended by "excrementitious vomiting." The hernia was opened and reduced. The patient had return of bowel function, but she died of asthma on the 17th postoperative day. Amyand emphasized that when the omentum interfered with reduction of a hernia, it should be amputated. A further sage observation is that if a hernia cannot be readily reduced it should be operated upon without delay. This course of action, he felt, would greatly improve results.

1745 (8)—He reported on a pathologic fracture of the humerus which occurred from muscle pull alone.

1745 (9)—He autopsied a 10 year old boy who died of intestinal obstruction. The description suggests a Meckel's diverticulum.

1746 (10)—On the treatment of osteomyelitis (spina ventosa), Amyand advocates earlier incision and drilling of the bone with a large opening. He recommended that if the disease reached a joint, then amputation should be done before overwhelming toxicity killed the patient.

Though he lived a full life in the professional world of London, Amyand found time to have a family of 3 sons and 6 daughters, most of whom went on to success, either via their own talents, or by judicious marriages. It is interesting to note that although he sired this large brood, the name of Amyand is no longer common in England. None of the children carried on the surgical tradition established by their father, but went into other fields to make their marks.

Claudius, Jr. took a B.A. from Oxford, he was subsequently an M.P. and in 1750 was Under-Secretary of State and a member of Lincoln's Inn. The third son, Thomas, took a B.A. and an M.A. from Oxford and entered the church.

George, the second son, became a prominent merchant and banker in London. He was a Director of the East India Company and the

Russia Company and was an M.P. from Barnstaple. He was created a baronet in 1764 and it is through his descendants that the family can be traced today. Sir George's son, George, married Catherine, daughter of Velters Cornewall, M.P. She was the only heir to the name and arms of Cornewall, George assumed the name of Cornewall, so the descendants of Amyand are now found under the name of Cornewall. The 7th Baronet is living today in Hereford (13).

Three of the daughters of Claudius were married; Anne to John Porter, M.P., Sheriff of London, Mary wed Sir Richard Adams, Recorder of London and Baron of the Exchequer, and Judith married the Rev. Thomas Ashton, D.D., Rector of St. Botolph, Bishopsgate.

One summer's day Sergeant-Surgeon Amyand went for a walk in Greenwich Park and by some mischance he fell and sustained a bruise, the site of which is unrecorded. He was carried to his home where he expired on the following day, July 6, 1740 (23). Amyand was about 55 years old at the time of his death, when after a full and occasionally stormy life, he quietly passed on to ill-deserved obscurity.

That Sergeant-Surgeon Amyand was moderately successful as a man of practical affairs is attested by his will (37), proved on July 9, 1740. He left to his wife Mary all his goods, his town house in Castle Street, and his country estates. To each of his children he left 1,000 pounds, and he devoted the sum of 300 pounds for putting out poor apprentices to business, possibly in remembrance of his own youth and apprenticeship.

His arms were "Vert a chev. betw. three garbs or . . ." Peachey says that neither bookplate nor portrait of Amyand has even been discovered. It is most odd that there is no record of a portrait; he certainly must have had one painted for one of his various offices, especially since the Masters of the Barber-Surgeons customarily had their portraits hung in the Hall. Amyand's living descendants today have no knowledge of the existence of a portrait or other memento of this notable 18th century surgeon.

SUMMARY

Here has been presented the story of the first recorded appendectomy, a tale too long ignored in medical annals, and the biography of the 18th century pioneer who had the temerity to do the operation which is today one of the most frequently performed.

Medical history has given credit to Mestivier of France for the first surgical attack upon the appendix. It has been shown here that Claudius Amyand of London performed the first successful recorded appendectomy on December 6, 1735, 22 years before Mestivier's unsuccessful incision and drainage of an appendiceal abscess.

The life of Amyand is a collection of bits and pieces; there is no complete extant record of the career of this surgical pathfinder. I have attempted to present the facts of the life of this surgeon who had a number of claims to fame, none of which has been sufficient to preserve his name, though he was Sergeant-Surgeon to King George II, pioneer in smallpox inoculation, Fellow of the Royal Society, first Principal Surgeon to the Westminster Hospital, a founder and first Principal Surgeon to St. George's Hospital, Master of the Barber Surgeons—one of the leading London surgeons of his day—and the first surgeon to do an appendectomy. Claudius Amyand was not a man of genius, but one of solid worth who merits a nod of recognition from medical history, too long denied him.

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REVIEWS OF NEW BOOKS

SOME time ago I reviewed for SURGERY, GYNECOLOGY AND OBSTETRICS the first fascicles of the *Atlas of Tumor Pathology*[1] which is being prepared for the Committee on Pathology of the National Research Council by its Subcommittee on Oncology and published by the Armed Forces Institute of Pathology. Now there are at hand the following additions: Section IV, Fascicle 14: *Tumors of the Thyroid Gland* by Shields Warren and William A. Meissner; Section IV, Fascicle 15: *Tumors of the Parathyroid Glands* by Benjamin Castleman; Section V, Fascicle 17: *Tumors of the Lower Respiratory Tract* by Averill A. Liebow; Section VIII, Fascicles 31B and 32: *Tumors of the Male Sex Organs* by Frank J. Dixon and Robert A. Moore; Section X, Fascicles 35 and 37: *Tumors of the Central Nervous System* by James W. Kernohan and George P. Sayre.

These fascicles are all models of concise organization and clear writing and are beautifully illustrated. They have been written by authorities on the different subjects and the manuscripts have been reviewed by the members of the Subcommittee on Oncology and by a group of special consultants, so that they can be assumed to represent adequately present knowledge of these tumors. It would be a mistake to give the impression that these fascicles are of use only to the pathologist, for there is much of value to the clinician, and especially to the practicing surgeon, in each of them. Each tumor is considered under the following headings: definition, gross pathology, microscopic pathology, histogenesis, natural history, differential diagnosis, and treatment.

Obviously in such a short space as is allowed to me in this review, it will be impossible to consider adequately these monographs. Therefore, I am merely pointing out the sections which have appeared to me to be particularly useful from a clinical point of view.

The classification of malignant tumors employed by Meissner and Warren has much to recommend it. Their use of descriptive terms, such as low grade localized carcinoma in follicular adenoma, and low grade localized carcinoma in papillary adenoma, should go far toward removing some of the confusion that has resulted from the employment of terms which are not understood in the same way by pathologists and clinicians.

The fascicle on parathyroid tumors is a concise review of the experience with these lesions at the Massachusetts General Hospital, where perhaps more of them have been studied than elsewhere in the world. Not only does Dr. Castleman consider the lesions in the parathyroid itself, but he also gives brief consideration of the lesions in the bone, kidney, and elsewhere.

Of particular interest are Dr. Liebow's discussions of bronchial adenoma and bronchiolar carcinoma (alveolar cell tumor). This fascicle on the tumors of the lower respiratory tract also contains a fine section on the cytology of the sputum. Dr. Liebow's interest in the clinical aspects of these tumors is reflected in his description of them in terms of specific bronchi and lung segments. This feature should be of considerable help to chest surgeons.

In the fascicle on the tumors of the male sex organs, I found particularly helpful the introductory chapter on carcinoma of the prostate. The section on testicular tumors is based on personal examination of one of the largest series of these tumors yet studied. The authors have also correlated the information gained by other workers who have examined a large series of testicular tumors. For additional information about these tumors, the fascicle of Willis on teratomas should be consulted. The present fascicle also contains a complete discussion of the interesting adenomatoid tumor of the epididymis.

The fascicle on tumors of the central nervous system, including the pineal body and meninges, employs a simplified classification of the gliomas and meningiomas. This procedure has much to recommend it and should be helpful to all who are concerned with the treatment of these tumors.

In closing this review of these splendid fascicles, it should be pointed out that their price is very low, thus making them one of the best book bargains on the market today. WILLIAM B. WARTMAN.

[1] ATLAS OF TUMOR PATHOLOGY. Published by the Armed Forces Institute of Pathology under the Auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council. Section IV, Fascicle 14: Tumors of the Thyroid Gland. By Shields Warren, M.D., and William A. Meissner, M.D. 97 pages, with 82 illustrations. $1.75. Section IV, Fascicle 15: Tumors of the Parathyroid Glands. By Benjamin Castleman, M.D. 74 pages, with 53 illustrations. $.65. Section V, Fascicle 17: Tumors of the Lower Respiratory Tract. By Averill A. Liebow, M.D. 189 pages, with 249 illustrations. $1.25. Section VIII, Fascicles 31b and 32: Tumors of the Male Sex Organs. By Frank J. Dixon, M.D., and Robert A. Moore, M.D. 179 pages, with 135 illustrations. $1.50. Section X, Fascicles 35 and 37: Tumors of the Central Nervous System. By James W. Kernohan, M.D., and George P. Sayre, M.D. 129 pages, with 126 illustrations. $.90. Washington, D.C., Armed Forces Institute of Pathology, 1952, 1953.

COMPRISING 150 pages *Die Lungenresektionen*[2] concerns itself with pulmonary resections, emphasizing the technical or surgical aspects. To this end it discusses all types of resection, bringing in as background only those clinical features which are pertinent from a purely technical standpoint. These include carcinoma and tuberculosis.

[2] DIE LUNGENRESEKTIONEN. By Prof. Dr. A. Lezius. With a preface by Prof. Dr. R. Nissen. 143 pages, with 149 illustrations. DM 49.80. Stuttgart: Georg Thieme, 1953.

The broad indications for pulmonary resection, as well as preoperative and postoperative handling and management during anesthesia, are developed to a limited extent.

The arrangement of the subject matter is logical and takes the reader through the technical aspects of right and left sided pneumonectomy, including intrapericardial dissection. Lobectomy likewise is presented by lobes and by sides as well as by combination of lobes, including even an azygos lobe. Segmental resections are well covered and graphically depicted. It is interesting to note that the local excision of lesions is done by circumferential dissection, securing by ligation all bronchi or vessels as they are found in the lung parenchyma. This technique is certainly to be preferred over wedge removal which utilizes clamps and leaves in many instances much crushed and distorted lung behind.

The large, flat format of this book is comfortable and convenient. The paper is of excellent quality, the print is clear, and the volume is profusely illustrated. These are, with two exceptions only, halftone stylized drawings. The standard incisions are described, but most of the surgical exposures as depicted show the lung as if viewed from a directly lateral axillary exposure.

Even though in the foreword the author indicates that this book represents examples of the situations which he has been called upon to care for, as well as a cross section of the problems encountered in the field, it must be assumed that this book will be used as an atlas or guide to the technical steps in various forms of pulmonary resection. Unfortunately it falls short of this goal. It is too condensed to be complete and too large to be truly sketchy. In trying to be succinct, the author has resorted to the expedient of interjecting into his illustrations, anomalous situations. Thus I find myself confronted with an anomalous anatomic situation when expecting to see the routine steps in a given resection. It would have done much for clarity had he given the standard anatomic steps and appended the usual variants as a separate presentation. Whereas this approach is resorted to, the other pattern remains disconcertingly fixed in my mind.

There is in evidence, also, considerable oversimplification, particularly of complex surgical maneuvers. Some of this is undoubtedly necessary; nevertheless such an approach is objectionable when it takes the form of gross idealization even to the point of being incompatible with everyday experience.

In discussing the problem of resecting the tracheal bifurcation the author's illustration shows the lung missing and the bronchus held by a clamp. Whereas it may be true that such a clinical situation will be encountered where the removal of the lung is a simple technical problem, leaving only the corynal resection as the chief point for consideration, this rarely is the case in actual practice. Furthermore, in carrying out the further steps he indicates by schematic drawings that not only is he willing to cut across the cancer once by removing the lung but a second time in order to insert an endobronchial tube into the remaining lung. Certain compromises can be made as calculated risks in technically difficult or almost impossible situations otherwise, but more or less blatantly to cut across a labeled carcinoma in an already idealized situation is shocking to me. Certainly a little more idealization would have eliminated this objectionable feature.

In repairing this defect, the author indicates as one method among others the use of a free bronchial graft obtained from the resected lung. I am again puzzled because it would indeed be rare that a piece of cancer free bronchus of such a size could be obtained from the specimen. I am much worried that such a forthright and simplified approach might bring an unwary operator into a situation from which it would be impossible for him to extricate himself.

Concerning the pattern of bronchial drainage in tuberculous cavities, he presents a full page multicolored plate of the right lung. He states that cavities in their spread do not respect segmental or lobar boundaries and shows a cavity in the anterior segment of the upper lobe communicating with the posterior segment of the upper lobe as well as the superior segment of the lower lobe. There is no argument that such can occur and often does, but the author fails to make clear the proposition that this is a compounded pathologic situation and, furthermore, he tends to abrogate the fact that the bronchopulmonary segment is a fundamental unit in all its aspects. Again the unwary man will be misled.

He also describes the operation of exposing the bronchus to an upper lobe, resecting a segment, and closing both sides in order to close a tuberculous cavity. One can envision only disaster from such an approach regardless of the clinical situation wherein it is applied.

The treatment of Pancoast tumors is likewise interesting because the author considers as inoperable those Pancoast tumors that involve the brachial plexus and resects those that do not. According to our definition only those tumors involving the structures in and about the thoracic inlet are called Pancoast tumors. The others are merely peripherally located lung tumors that invade the chest wall below the thoracic inlet.

It is obvious that I am focusing my attention on illustrations, but if this book is to be put to any practical use it is as a guide or atlas, and it is commonly agreed that illustrations assume tremendous importance under these circumstances. Oversimplification, erratic presentation of anomalies, and the apparent facility with which idealization is undertaken are confusing to me. To the patient of a more or less inexperienced operator bold enough to tackle the problem of pulmonary resection they might well bring about disaster.

HIRAM T. LANGSTON.

THE second edition of George P. Pitkin's *Conduction Anesthesia*,[1] edited by James L. Southworth, Robert Hingson, and Winifred M. Pitkin, is a massive volume of approximately 1,000 pages. It is a work which should be of interest to both the novice and the expert in the field of conduction anesthesia. The novice will find it valuable because it emphasizes that exact anatomic knowledge, proper equipment, and a thorough understanding of drugs are prerequisite to success in conduction anesthesia. The expert will find the exhaustive discussion of methods and the anatomic drawings useful for reference purposes.

The first chapter is devoted to exposing the fallacies in some techniques which have been copied from textbook to textbook over the years.

In the next four chapters the authors give a detailed description of the anatomy of the nervous system together with many excellent illustrations. The anatomic section is written solely with the purpose of being useful to the practitioner of conduction anesthesia, and these chapters bring together in one volume anatomic information that is usually found with difficulty by reading in scattered scources.

The pharmacology of local anesthetic agents, plus several valuable tables listing the properties of these drugs, form the next two chapters.

Chapter VII defines the various types of conduction anesthesia in an effort to clear up much fuzzy thinking and stop the use of improper terms by many surgeons. In this chapter, also, the authors discuss the fundamental principles of technique common to all forms of conduction anesthesia. The special needles and syringes which are so essential to success in this work are enumerated and carefully described.

Chapter VIII through Chapter XIV describe in detail the methods used to produce anesthesia in every part of the body. The reader is given a wide choice of methods, but the authors take care to point out the advantages and disadvantages of each and to list the particular techniques with which they have had the most success. The illustrations in this section are excellent and supplement those of the anatomical section of the book.

The final portion of the book contains chapters on local anesthesia, topical and refrigeration anesthesia, extradural anesthesia, and spinal anesthesia. The volume ends with chapters on the therapeutic uses of conduction anesthesia, and complications of conduction anesthesia. The discussion of complications is presented with refreshing frankness and helps one to evaluate more properly these methods in relation to other forms of anesthesia.

The reader may not agree with everything in the book since the authors are obvious enthusiasts but it should stimulate him to do a lot of thinking. It is a volume which should be read by anyone who does surgery or practices conduction anesthesia.

JOHN W. HIRSHFELD.

[1]CONDUCTION ANESTHESIA. By George P. Pitkin, M.D., F.A.C.S., F.I.C.A. Edited by James L. Southworth, Robert A. Hingson, and Winifred M. Pitkin. 2nd ed. 1,005 pages, with 585 illustrations. $22.50. Philadelphia, London, Montreal: J. B. Lippincott Co., 1953.

ALL of the papers presented at the Surgical Forum of the American College of Surgeons' meeting in New York, September 1952 are presented in one volume.[2] The Surgical Forum is specifically designed to present the experimental and clinical investigative studies of young surgeons throughout the United States and Canada. The papers included in this volume represent the results of intensive basic research in the many laboratories of these two countries. As a result of the publication of such work, a better understanding of the pathologic physiology of surgical disease can be expected. In view of the extensive surgical research being accomplished on the American continent, it is obvious that even the most recent of textbooks cannot possibly contain the latest advancements in surgery. Herein lies the value of such a volume as the *Surgical Forum* of the American College of Surgeons.

In spite of the recent interest in the surgery of the heart and great vessels, the Surgical Forum Committee has properly seen fit to emphasize basic experimental investigative studies in other areas of the body where surgical research has been accomplished. The sections on the stomach include not only papers on the disturbed physiology of the stomach with respect to surgical procedures on that organ, but also clinical studies on large series of patients who have received various types of operative procedures on the stomach. New types of gastric resection techniques for duodenal ulcer as well as studies on the replacement of the stomach by other segments of the gastrointestinal tract are included.

The section on the experimental studies concerning the heart and great vessels is of necessity of considerable length. The interest regarding the surgical approach to these areas in recent years explains the multitude of basic surgical research papers. It is stimulating, however, to note that in this volume emphasis is placed not on surgical techniques with respect to the various surgical procedures involved, but rather upon the basic physiologic and pathologic disturbances incident to the congenital or acquired defects noted within the cardiac chambers or within the great vessels immediately beyond them. The metabolic changes associated with the various pump-oxygenator mechanisms are discussed and certain insight is gained into their knowledge.

[2]SURGICAL FORUM: PROCEEDINGS OF THE FORUM SESSIONS THIRTY-EIGHTH CLINICAL CONGRESS OF THE AMERICAN COLLEGE OF SURGEONS, NEW YORK CITY, SEPTEMBER, 1952. Surgical Forum Committee: Owen H. Wangensteen, M.D., F.A.C.S., Minneapolis, Chairman, J. Garrott Allen, M.D., F.A.C.S., Chicago, Warren H. Cole, M.D., F.A.C.S., Chicago, Robert E. Gross, M.D., F.A.C.S., Boston, Carl A. Moyer, M.D., F.A.C.S., Dallas, I. S. Ravdin, M.D., F.A.C.S., Philadelphia, and H. B. Shumacker, M.D., F.A.C.S., Indianapolis. 716 pages, illustrated. $10.00. Philadelphia, London: W. B. Saunders Co., 1953.

The results of hemodynamic studies performed during mitral valve surgery are described as well as a technique for producing mitral stenosis of a controlled degree. The effect of pH changes on vagal inhibition of the heart as well as factors influencing survival in experimental cardiac tamponade are discussed. The experimental closure of atrial septal defects by the use of an atrial well is described. All of the papers represent significant advancements in the technique and the understanding of cardiac surgery.

Further sections are concerned with pathologic and physiologic studies in the fields of gynecology and obstetrics, anesthesia, shock, plastic surgery, water balance and electrolytes, and there is a rather large section on portal hypertension, liver, pancreas, and blood coagulation.

It must be emphasized that the material included in this volume is concerned mainly with laboratory investigations of fundamental surgical problems and indicates the influence of basic surgical research on therapy of the future, for it is mainly on the basis of the surgical experience in the laboratory that further advances in therapy will occur. As the result of such work, a better understanding of the pathologic physiology of many surgical diseases has become possible. It is likewise true that, as a result of these investigations, many operations previously considered impossible have now become commonplace procedures. ORVILLE F. GRIMES.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

HANDBOOK OF DIFFERENTIAL DIAGNOSIS. By Harold Thomas Hyman, M.D. 716 pages. $6.75. Philadelphia, London, Montreal: J. B. Lippincott Co., 1953.

INJURIES OF THE SPINAL CORD. Edited by George C. Prather, M.D., F.A.C.S., and Frank H. Mayfield, M.D., F.A.C.S. 396 pages, 125 illustrations. $8.75. Springfield, Ill.: Charles C Thomas, 1953.

ADVANCES IN PEDIATRICS. Edited by S. Z. Levine. Associate Editors, John A. Anderson, Margaret Dann, L. Emmett Holt, Jr., A. Ashley Weech, and Myron E. Wegman. Vol. 6. 323 pages, illustrated. $7.50. Chicago: The Year Book Publishers, Inc., 1953.

A PRACTICE OF THORACIC SURGERY. By A. L. d'Abreu, O.B.E., Ch.M., F.R.C.S. 591 pages, illustrated. London: Edward Arnold & Co.; Baltimore: The Williams & Wilkins Co., 1953.

THE OBSTETRICAL FORCEPS. By L. V. Dill, M.D., F.A.C.S. 145 pages, 86 illustrations. $5.25. Springfield, Ill.: Charles C Thomas, 1953.

LIVING WITH A DISABILITY. By Howard A. Rusk, M.D., and Eugene J. Taylor in collaboration with Muriel Zimmerman, O.T.R., and Julia Judson, M.S. 207 pages, 281 illustrations. $3.50. Garden City, N. Y.: The Blakiston Co., Inc., 1953.

ANNUAL REPORT ON THE RESULTS OF TREATMENT IN CARCINOMA OF THE UTERUS. 8th vol. Statements of Results Obtained in 1946 and Previous Years (Collated in 1952). Sponsored by American Cancer Society, British Empire Cancer Campaign, Cancerfoereningen, Stockholm, Damon Runyon Memorial Fund, New York, Landsforeningen mot Kreft, Oslo, National Cancer Institute of Canada. Dr. J. Heyman, Editor. Stockholm: The Editorial Office, Annual Report, Radiumhemmet.

SEXUAL BEHAVIOR IN THE HUMAN FEMALE. By the Staff of the Institute for Sex Research, Indiana University. Research Associate, Alfred C. Kinsey, Wardell B. Pomeroy, Clyde E. Martin, Paul H. Gebhard. 842 pages, 155 illustrations. $8.00. Philadelphia and London: W. B. Saunders Co., 1953.

DIVERTICULOSIS Y DIVERTICULITIS DEL COLON: MORFOPATOLOGIA, DIAGNOSTICO, TRATAMIENTO. By Abel N. Canonico, M.D. 216 pages 120, illustrations. Buenos Aires: Libreria "El Ateneo" editorial, 1953.

MANUAL OF MEDICAL EMERGENCIES. By Stuart C. Cullen, M.D., and E. G. Gross, M.D. 2nd ed. 278 pages, 34 illustrations. $4.50. Chicago: The Year Book Publishers, Inc., 1953.

OBSTETRICIA PRACTICA: PRESENTACION PELVIANA. By Prof. Juan Leon. 255 pages, 211 illustrations. Buenos Aires: Libreria "El Ateneo" editorial, 1953.

SURGICAL TECHNIQUE AND PRINCIPLES OF OPERATIVE SURGERY. By A. V. Partipilo, M.D., F.A.C.S. 704 pages, 548 illustrations. $15.00. Philadelphia: Lea & Febiger, 1953.

THE PHYSICS OF RADIATION THERAPY. By Harold Elford Johns, M.A., Ph.D., F.R.S.C. 286 pages, illustrated. $8.50. Springfield, Ill.: Charles C Thomas, 1953.

THE ROCKEFELLER FOUNDATION; ANNUAL REPORT 1952. 465 pages, illustrated. New York: The Rockefeller Foundation, 1953.

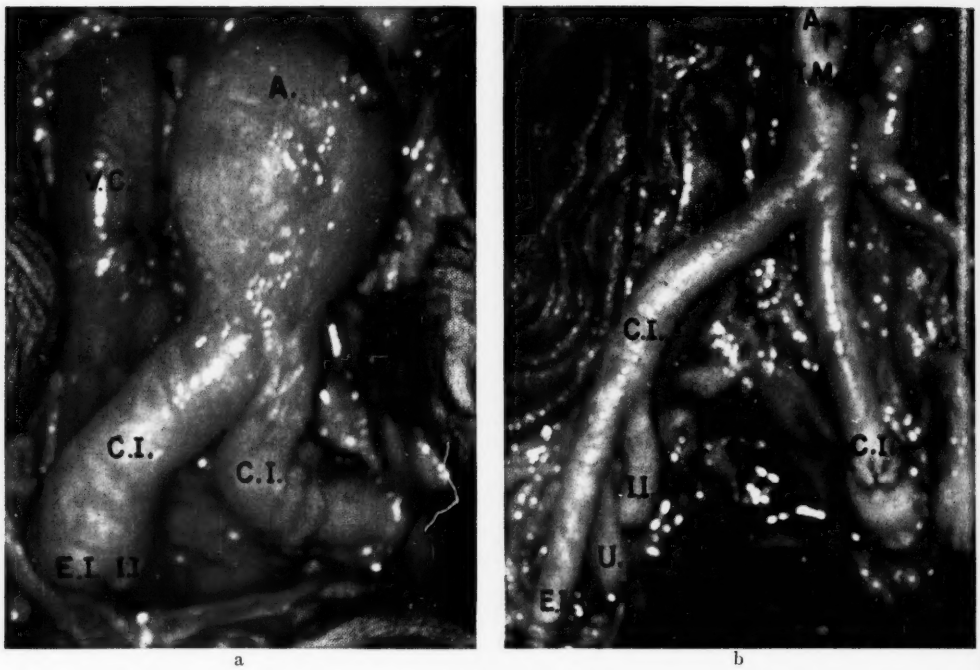
A HANDBOOK FOR DISSECTORS. By J. C. Boileau Grant, M.D., and H. A. Cates, M.D. 4th ed. 425 pages, 26 illustrations. $3.50. Baltimore: The Williams & Wilkins Co., 1953.

MODERN TRENDS IN UROLOGY. Edited by E. W. Riches, M.C., M.S., F.R.S.C. With a foreword by the Lord Webb-Johnson, K.C.V.O., C.B.E., D.S.O., T.D., M.B., LL.D., F.R.C.S. 476 pages, 215 illustrations. $12.50. New York: Paul B. Hoeber, Inc. Medical Book Department of Harper & Brothers, 1953.

ZWANGLOSE ABHANDLUNGEN AUF DEM GEBIETE DER FRAUENHEILKUNDE. Edited by Prof. Dr. Robert Schröder. Vol. 15. Oxydationslage und Eiweiss-stoffwechsel bei Schwangerschaftstoxikosen. By Dozent Dr. med. habil. Helmut Kyank. 102 pages, 42 illustrations. DM 12. Leipzig: George Thieme, 1953.

COMPRESSION ARTHRODESIS: INCLUDING CENTRAL DISLOCATION AS A PRINCIPLE IN HIP SURGERY. By John Charnley, F.R.C.S. $8.50. 264 pages, 208 illustrations. Edinburgh and London: E. & S. Livingstone Ltd., 1953. Baltimore: The Williams & Wilkins Co., 1953.

HYPERPARATHYROIDISM. By B. Marden Black, M.D. 119 pages, 19 illustrations. $3.75. Springfield, Illinois: Charles C Thomas, 1953.



a b

Fig. 8. a, Aneurysmal dilatation of the aorta (*A*) beginning approximately 4 centimeters below the renal arteries and extending on the right into the common iliac (*CI*) and the external (*EI*) and internal (*II*) iliac arteries. The aneurysm involves the common iliac (*CI*) artery on the left. b, The freeze-dried graft after completion of the anastomoses. The aortic portion (*A*) is shown with the ligated inferior mesenteric artery (*IM*). The aortic anastomosis is above the area included in the photograph. The right external (*EI*) and internal iliac (*II*) anastomosis are shown. The ureter (*U*) has been transplanted to lie between the two vessels. The common iliac anastomosis (*CI*) is shown on the left.